APPENDIX A

STUDY DESCRIPTIONS AND DATA SUMMARIES

Appendix A provides a summary of each of the epidemiological studies retained for use in the model fitting effort for lung cancer and/or mesothelioma. Each description is organized into three main parts:

- List of citations. This lists the citation that is the primary source of quantitative exposure response data, along with any other publications on the same cohort that provide additional information that is helpful in understanding each study.

- Study description. This section summarizes the most important attributes of each study, including a description of the exposure setting, the type of asbestos in the workplace air, the cohort that was observed, and the data resulting from the study.

- Assessment of bias and uncertainty. This section describes the sources of uncertainty and/or bias in the data from each study, along with the probability density functions (PDFs) selected to characterize the uncertainty or account for the bias. These PDFs are selected in accord with the general strategies discussed in Appendix C.

The data used in the model fitting are presented in tabular and graphical format at the end of each section. The uncertainty bars around each data point represent the 95% confidence limit based only on Poisson uncertainty around the observed number of cases.

Sections in This Appendix

Section	Cohort
A1	British friction product factory
A2	South Carolina textile workers
A3	Retirees from a U.S asbestos company
A4	Ontario cement manufacturers
A5	New Orleans cement manufacturers
A6	Quebec chrysotile miners
A7	Pennsylvania textile workers
A8	Connecticut friction product workers
A9	Rochdale England textile workers
A10	Italian chrysotile miners
A11	New Jersey insulation manufacturers
A12	Swedish cement manufacturers
A13	Libby Montana vermiculite miners
A14	Australian crocidolite miners
A15	Belgian cement manufacturers
A16	Austrian cement manufacturers
A17	Chinese workers in a mixed-product factory

A1. British Friction Products Plant

References

Primary: Berry, G., and Newhouse, M. (1983). Mortality of workers manufacturing friction materials using asbestos. *British Journal of Industrial Medicine*, **40**: 1-7.

Other: Newhouse, M., Berry, G., and Skidmore, J. (1982). A mortality study of workers manufacturing friction materials with chrysotile asbestos. In: Walton, W., eds. *Inhaled Particle V*. Oxford: Pergamon Press, pp. 889-909.

Newhouse, M., and Sullivan, K. (1989). A mortality study of workers manufacturing friction materials: 1941-86. *British Journal of Industrial Medicine*, **46**: 176-179.

Berry G. 1994. Mortality and cancer incidence of workers exposed to chrysotile asbestos in the friction-products industry. Ann. Occup. Hyg. 38:539-546.

Berry G. 1980. Dose-response in case-control studies. J. Epidemiol. Community Health 34:217-222.

Skidmore, J.W., and Dufficy, B. (1983). Environmental history of a friction material factory. *British Journal of Industrial Medicine*, **40**: 8-12.

Study Description

Location and Facility Description

The Ferodo factory is located in the United Kingdom. The factory has manufactured brake blocks, brake and clutch linings, and other friction materials continuously since it was opened in 1898. Use of woven asbestos in these products began about 1910, and by 1920 was the dominant material used. This woven material was produced off-site, and no asbestos textile operations ever occurred in the factory. In 1922, use of non-woven asbestos in brake blocks was begun, although use of woven asbestos continued to be the primary form. The main processes carried out in the factory have been a) forming resin-based blocks that contain asbestos, b) forming the blocks into the required shapes, and c) machining or grinding the blocks (Newhouse et al. 1982).

Asbestos Type

Chrysotile asbestos was used almost exclusively at the plant except during two relatively short periods (1929-1933 and 1939-1944) when crocidolite was used specifically in the production of railway blocks. The use of crocidolite was limited to a well-defined area of the factory, and only a minority of the work-force was exposed in this area. Berry and Newhouse (1983) also report that “very small quantities” of crocidolite were used in the experimental workshop on occasion, although there is no description as to the exposure of the workforce within this workshop.

Fraction Amphibole

Because the cohort evaluated in this report included workers who were employed in 1941 and after, it is likely that some individuals in the cohort were exposed to crocidolite during the 1939-1944 time interval, and possibly in the 1929-1933 time interval. The authors do not provide any data on the relative amounts of crocidolite used, or on the fraction of the workforce who may have been exposed in the sub-area of the factory producing crocidolite-containing railway blocks. In the absence of data, it is very difficult to judge the extent to which exposure to crocidolite may have occurred in this workforce and contributed to the observed health effects, but the authors seem to imply that the contribution is small. Therefore, a screening level value of 0.5% is assumed for the average fraction amphibole in the workplace. As discussed below, this value is considered to be quite uncertain.

Cohort Description and Follow-up

Berry and Newhouse (1983) evaluated the mortality experience of 13,460 subjects employed at the British friction products plant between 1941 and 1977, of which about two-thirds were men. Personnel files were incomplete for 35 subjects. The total number of person-years was not reported. About 50% of the workforce was less than 24 years of age when first employed at the factory, and women on average started working at a younger age than the men. Approximately 16% of the workforce had one or more breaks in their employment at the British factory, while the rest of the men and women worked for a continuous period. Almost one-third of the workforce left the factory after a year of service, while 27% of the men and 14% of the women remained employed for over 10 years.

Follow-up was carried out to the end of 1979. Only 0.67% of the individuals included in this cohort were lost to follow-up. Over two-thirds of the workers began employment prior to 1960, and as such would have been followed up for at least 20 years since their first exposures. During the follow-up through 1979, a total of 2,173 deaths (all causes) were registered (Berry and Newhouse 1983). Follow-up was extended another seven years to 1986, recording a further 769 deaths (Newhouse and Sullivan 1989). However, the data in this follow-up report were not stratified according to cumulative exposure, so only the data from Berry and Newhouse (1983) were used in this evaluation.

Determination of Cause of Death and Diagnosis of Lung Cancer/Mesothelioma Cases

Causes of death for members of the cohort were obtained through the Office of Population Censuses and Surveys (OPCS) and the Department of Health and Social Security (DHSS). The cause of death was coded according to the 8th revision of the International Classification of Diseases (ICD).

Reference Population

Berry and Newhouse (1983) compared the observed mortality of the friction product cohort with that expected computed from period-specific death rates for England and Wales based on sex and age.

Estimating Exposure Concentration

Beginning in 1967, regular sampling of workplace air was performed using the PCM method. Personal sampling began in 1968. Fiber concentrations in earlier years were estimated by reproducing earlier working conditions based on detailed knowledge of the environment at the time including when processes were changed and introduction of exhaust ventilation (Skidmore and Dufficy, 1983). During the simulation of earlier conditions, personal and stationary air measurements were collected. Values estimated by the authors are summarized below:

Mean Asbestos Concentration (f/cc)

Time period	Location			
	Office/laboratory	Storage/distribution	Grinding	Forming
Pre 1931	10-20	>20	>20	>20
1932-50	<0.5	2-5	5-10	2-5
1951-69	<0.5	2-5	2-5	1-2
1970-79	<0.5	0.5-1	0.5-1	0.5-1

Source: Berry and Newhouse (1983) (Table 1).

Estimating Cumulative Exposure

Occupational histories were extracted from employee personnel files and used to estimate levels of cumulative exposure for each individual. The personnel filing system was first instituted at the factory in 1941. Workers who were first employed prior to 1941 and who left before implementation of the filing system were excluded from the analysis. Thirty-five additional subjects were excluded due to incomplete identity information.

Smoking Data

Berry and Newhouse (1983) were not able to collect enough data to evaluate smoking prevalence in this cohort. However, the authors stated that the workers demonstrated a reduction in smoking compared to the national population. This may tend to diminish the absolute magnitude of an asbestos effect on lung cancer incidence, but the authors state that it was unlikely to distort a dose-exposure relationship within the factory.

Lung Cancer Results

The dose-response relationship between chrysotile exposure and lung cancer (ICD 162) was evaluated by Berry and Newhouse (1983) with a case-control study. Of those subjects evaluated for overall mortality, only men who began work after 1941 but prior to 1960 who survived for at least 10 years after starting work in the factory were included in this analysis. Three controls were matched to each case based on birth year, the year of start of employment and survival up to time of death (of the case) from lung cancer. Ninety-seven percent of the controls were matched to within four years with the cases. From data presented in Table 12 of Berry and Newhouse (1983), 106 cases and 317 controls were included in the analysis. One control was omitted due to missing information on the person’s occupational history. Occupational histories were used to estimate cumulative exposure up to the date of death for the cases, and up to the date of death of the corresponding case of lung cancer for the controls.

Berry and Newhouse (1983) fit a linear exposure model relating cumulative exposure and lung cancer to case-control data using methods appropriate to matched data (Berry 1980). The estimated lung cancer potency factor (KL) estimated using this method was 5.8E-04 $(f/mL\text{-}yr)^{-1}$. The relative risk was estimated to be 1.06 for a cumulative exposure of 100 f/mL-yr, with an upper 90% confidence limit of 1.80.

The mortality data are presented in Table 14 of Berry and Newhouse (1983) and are presented in Figure A1-1 below. Because the incidence of lung cancer is expected to be low in both cases and controls, the odds ratio was taken as a reasonable approximation of the relative risk. As seen, the data do not reveal an increasing dose-response trend for lung cancer over the range of exposures studied. The authors also found no indication of increased risk with duration of exposure.

Berry and Newhouse (1983) also evaluated lung cancer risk by excluding the nine most recent years of exposure, and by weighting each subject's cumulative dose by their time since last exposure. These data are not presented, but the authors state that there was no sign of increased risk with duration or cumulative exposure based on either of these measures.

Mesothelioma Results

Berry and Newhouse (1983) reported 10 deaths within the total cohort from pleural mesothelioma. A case control study was performed to investigate the potential role of exposure to crocidolite in the occurrence of these cases. Controls were matched based on year of first employment, gender, year of birth, survival up to time of death, and employment during the period of time when crocidolite was used. Four controls were matched to each case. An additional death from mesothelioma was noted after the end of the follow-up period in a 50-year old man known to have worked at the factory for two weeks in 1960 (age 29). His only known exposure was to chrysotile asbestos in the friction product factory.

Work histories for eight of the cases (and their matching controls) were not available and job histories could only be established through employee interviews. Nine of the cases were employed during at least one of the periods when crocidolite was used. Eight of them had definite exposure to crocidolite (known to have worked on the crocidolite contract), and one had "fringe" exposure (more than 15-m from crocidolite work or chance intermittent exposure). Eighty percent of the mesothelioma cases had worked directly on the crocidolite contract, compared with only 8% of the controls. It was also found that the cases of mesothelioma were in subjects that had also been exposed to higher levels of chrysotile asbestos than the controls. One case of mesothelioma had previous exposure in a cement factory. However, no data on incidence as a function of cumulative exposure were presented, so these results were not included when fitting the quantitative mesothelioma exposure-response model.

Uncertainty and Bias Characterization

Appendix C discusses the primary sources of uncertainty in epidemiological studies of cancer risk from asbestos exposure in the workplace and describes the methods used in this document for characterizing the uncertainty. The following sections discuss the uncertainty characterization and issues of potential bias for this study.

Uncertainty Due to Measurement Error

As described in Section 3.1 of Appendix C, all estimates of concentration levels of asbestos in the workplace are uncertain due to the combination of sampling error and analytical error. These measurements are usually averaged according to job or work area, often stratified by time. For this study, Berry and Newhouse (1983) report mean concentrations as a function of time period and operation (see Table 1 in the original report). The magnitude of the uncertainty in the reported mean value for each job/time category (which is used to compute cumulative exposure) is a function of a) the number of samples used to compute the mean, b) the between-sample variability, and c) the nature of the underlying distribution. However, the authors do not provide information on the number of samples collected, or on the degree of between-sample variability. Therefore, in the absence of data, the default assumption described in Appendix C is applied to this study to account for measurement error, and is characterized as:

PDF(measurement error) ~ TRI(0.6, 1, 1.5)

Uncertainty in Mean Values for Exposure Groups

For lung cancer, the point estimate of CE10 is based on the mid-point of the reported exposure range. In accord with the general approach described in Appendix C, this point estimate is an uncertain estimate of the true mean, and the uncertainty is characterized as follows:

PDF(exposure, bounded) ~ TRI(Min/Mid, 1, Max/Mid)

Uncertainty in Conversion Factor (CF) from Dust Data (mppcf) to PCM f/cc

In this study, workplace air measurements did not occur until 1967. These measurements were made using the membrane filter method using PCM-based counting rules. Thus, no uncertainty factor is needed to account for extrapolation from dust to fiber concentrations.

Uncertainty in the Use of Stationary Rather Than Personal Air Monitors

As mentioned above, measures of asbestos in air were regularly collected beginning in 1967 and personal sampling began in 1968. Estimates for the period prior to 1967 were collected under simulated conditions using both personal and stationary air monitors. Static measurements were collected primarily to provide an understanding of the general atmospheric contamination (Skidmore and Dufficy 1983). The authors do not state whether or not the exposure estimates were based only on the personal air measurements, or on both the personal and stationary measurements. Personal samplers provide a better estimation of the concentration values associated with each worker's exposure. Since personal measurements were collected, it is assumed that the author's would have based the exposure estimates primarily on these measurements. As such, no uncertainty factor is applied to this study to account for the use of stationary air monitors.

Uncertainty in Temporal Representativeness

For the British friction products factory, PCM measurements are available from 1967 onward. As mentioned above, estimates of exposure prior to 1967 were based on attempts to recreate exposure conditions using original machines based on knowledge of when major changes in industrial hygiene occurred in the factory. The cohort evaluated by Berry and Newhouse (1983) was defined as those workers employed in or after 1941 up to 1977. Thus, measurements are missing for a considerable portion of the cohort, but concentrations are estimated for the most part from simulated conditions. Based on this, uncertainty in temporal representativeness is ranked as medium, and is characterized by:

PDF(temporal representativeness) ~ TRI(0.8, 1, 1.2)

Bias Correction Factor in Data Reported as CE Rather Than CE10

This study reports cumulative exposure as CE rather than as CE10. As discussed in section 3.6 of Appendix C, use of CE rather than CE10 tends to bias results low, with the magnitude depending on the duration of exposure, the length of follow-up, and whether or not early person years of observation were excluded. Berry and Newhouse (1983) does not report the average duration, but data presented in table 5 of the study indicate that nearly 40% of the workforce was employed for less than 5 years, and only 11% worked for 20 years or more. Therefore, an average duration of 5 years was assumed within a range between 1 and 30 years. As described above, the lung cancer mortality data based on the case-control study did not exclude any person-years of observation. Based on these study attributes a BCF for this cohort was determined to be:

BCF ~ TRI(1.5, 1.7, 1.9)

Uncertainty in Fraction Amphibole

As noted above, workers in this factory were primarily exposed to chrysotile asbestos. However, crocidolite was also used for two specified periods in the production of railway blocks, and occasionally in the experimental workshop. No data were reported on the relative amounts of amphibole present, or on the fraction of the workforce that would have been exposed to crocidolite. In the absence of data, it is considered likely that f_{amph} must be small, although the relative uncertainty around the value is large. Based on professional judgment, the following PDF is selected for use:

PDF(f_{amph}) ~ TRI(0, 0.005, 0.02)

Uncertainty in Particle Size Data for Chrysotile

For this study, the primary type of asbestos used at the friction products factory was chrysotile. Of the TEM data sets available (see Appendix B), 11 are based on chrysotile asbestos, three of which correspond to the friction products industry. These data sets differ by operation as mixing, forming, and finishing. As the exposure groups evaluated by Berry and Newhouse (1983) are not categorized by operation, there is no basis for selecting any one data set over the other. The three chrysotile friction product TEM data sets were combined. Since the assigned TEM data sets match on asbestos type and industry, the uncertainty in f_{size} for chrysotile is determined to be low for this cohort and is characterized by:

PDF($f_{size[chrysotile]}$) ~ TRI(0.8, 1, 1.2)

Uncertainty in Particle Size Data for Amphibole

Of the TEM data sets available (see Appendix B), 18 are based on amphibole asbestos, but none are based on samples from the friction products industry. Crocidolite was the type of amphibole asbestos used for a short period of time at the British friction products factory, so all TEM data sets based on crocidolite were combined to estimate the size distribution for amphiboles. In accord with the general approach described in Appendix C, when the TEM data set matches on amphibole type but not industry, uncertainty is ranked as medium and is characterized by:

$$PDF(f_{size[amphibole]}) \sim TRI(0.5, 1, 1.5)$$

Figure A1-1. Raw Lung Cancer Data for the British Factory

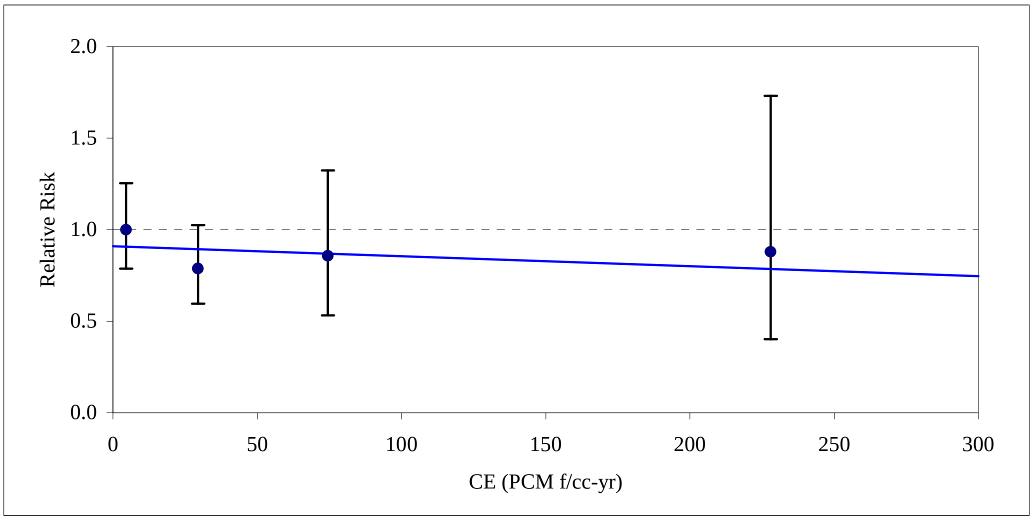
CE (PCM f/cc-yr)		Controls (a)	Cases (a)	Expected Deaths (c)	Odds Ratio (d)		
Range (a)	Mean (b)				Pt. Est. (a)	5% LB	95% UB
0-9	4.5	132	50	50	1.0	0.8	1.3
10-49	29.5	124	37	47	0.8	0.6	1.0
50-99	74.5	40	13	15.2	0.9	0.5	1.3
100-356	228	15	5	5.7	0.9	0.4	1.7

a) Reported in Table 14 (Berry and Newhouse 1983).

b) Calculated as the midpoint of the reported range.

c) Expected deaths = cases/odds ratio

d) OR approximates RR when incidence is low, as in the case of lung cancer.



A2. South Carolina Textile Plant

The South Carolina textile worker cohort has been studied by two different groups led by J.M. Dement and A.D. McDonald. The data from these two different groups are presented separately, below.

Studies by Dement et al.

Primary: Hein, M.J., Stayner L., Lehman E., and Dement, J.M. 2007. Follow-up study of chrysotile textile workers: Cohort mortality and exposure-response. *Occup. Environ. Med.* Published on-line odoi:10.1136/oem.2006.031005.

Other: Dement, J., Brown, D., and Okun, A. (1994). Follow-up study of chrysotile asbestos textile workers: cohort mortality and case-control analyses. *American Journal of Industrial Medicine* **26**:431-447.

Dement, J., Harris, R., Symons, M., and Shy, C. (1982). Estimates of dose-response for respiratory cancer among chrysotile asbestos textile workers. *Ann. Occup. Hyg.* 26:869-887.

Dement, J., Harris, R., Symons, M., and Shy, C. (1983a). Exposures and mortality among chrysotile workers. Part I: Exposure Estimates. *American Journal of Industrial Medicine* **4**:399-419.

Dement, J., Harris, R., Symons, M., and Shy, C. (1983b). Exposures and mortality among chrysotile workers. Part II: Mortality. *American Journal of Industrial Medicine* **4**:421-433.

Dement, J. and Brown, D. (1998). Cohort mortality and case-control studies of white male chrysotile asbestos textile workers. *Journal of Clean Technology, Environmental Toxicology, and Occupational Medicine* **7**(4):413-419.

Study Description

Location and Facility Description

The plant was located in Charleston, South Carolina. Production of asbestos packing materials for steam engines and pumps began in 1896, and production of asbestos textiles (yarn and cloth) began in 1909 (Dement et al. 1983a). Textile production operations were concentrated in five buildings, typically one or two stories tall. The plant was considered to be progressive in the application of dust control measures, and an assessment performed in 1937 by the Public Health Service (PHS) concluded that the dust control practices were "representative of the best practices in this country at this time" (Dement et al. 1983a). After the PHS study in 1937, several additional exhaust ventilation systems were installed to further reduce exposures in certain processing areas (Dement et al. 1983a). The plant stopped using asbestos material by the end of 1977 (Hein et al. 2007).

Asbestos Type

Chrysotile asbestos was the primary material processed at the plant for textile production (Dement et al. 1983a, Hein et al. 2007). The chrysotile asbestos used by the plant was received from Quebec, British Columbia, and Rhodesia. Small quantities of crocidolite yarn were also used at the plant to make tape or braided packing from the 1950s to 1975. However, only 2,000 pounds of crocidolite was used over this period, compared to the 6-8 million pounds per year of chrysotile used during the same period (Dement et al. 1983a, Hein et al. 2007).

Fraction Amphibole

Based on the reported amount of crocidolite used (2000 pounds total between 1950 and 1975), the amount used per year (less than 100 pounds/yr) is very small (about 0.001%) compared to the amount of chrysotile used (6-8 million pounds/yr). Moreover, the crocidolite used in the factory was never carded, spun, or twisted (Dement et al. 1983a), so release of fibers from the crocidolite into air was likely lower than for chrysotile. However, as discussed in Appendix C, chrysotile is often contaminated with trace levels of tremolite amphibole. Based on the data summarized in Appendix C, the estimated average level of amphibole in chrysotile is 0.054%.

Cohort Description and Follow-up

In the first study of this plant (Dement et al. 1982, 1983a, 1983b), the cohort was defined as all white male workers who worked for at least one month between 1940 and 1965. Follow-up was through December 31, 1975. In a subsequent report, Dement et al. (1994) expanded the cohort to 3,022 people, including non-white male and white female workers who met the entrance requirements, and extended follow-up an additional 15 years (through December 31, 1990). In the most recent update (Hein et al. 2007); the cohort was increased by the addition of 21 non-white females and 29 workers who had previously been lost to follow-up. Thus, the cohort evaluated by Hein et al. (2007) consisted of 3,072 workers (1,256 white males, 1,244 white females, 551 non-white males, and 21 non-white females), with follow-up through 2001. This provided 118,513 person-years of observation.

Determination of Cause of Death and Diagnosis of Lung Cancer/Mesothelioma Cases

In the cohort described by Hein et al. (2007), a total of 1,961 deaths (64% of the cohort) were identified. Cause of death was ascertained by submitting names of cohort members to the National Death Index (NDI), which provided vital status and cause of death data, coded according to the International Classification of Diseases (ICD) in effect at the time of death. Cause of death data were obtained from the NDI for all but 120 individuals. The authors reviewed death certificates for any mention of mesothelioma to identify pleural and peritoneal mesothelioma deaths occurring between 1991 and 1998. Deaths from mesothelioma occurring after 1998 were coded according to the tenth revision of the ICD (ICD-10) and were identified with the code C45 in the NDI cause of death file.

Reference Population

United States mortality rates specific for each race and sex group were used to calculate expected deaths by cause. For comparative purposes, analyses were also completed using South Carolina death rates (Hein et al. 2007). South Carolina rates were not available prior to 1960, so those deaths occurring prior to that date were not included in that calculation.

Estimating Exposure Concentration

Exposure estimates used by Hein et al. (2007) were previously described by Dement et al. (1983a). A total of 5,952 environmental samples were collected from the plant during the period covering 1930-1975. From 1930-1965, measurements were collected using midget impingers. Both impinger measurements and membrane filter samples were collected from 1965 until 1971. After 1971, only the membrane filter method was used.

Conversion of impinger measurements (mppcf) into units of PCM f/cc was based on a site-specific analysis of the relationship between paired and concurrent measurements. Dement et al. (1983a) found that a conversion factor of 2.5 PCM f/cc per mppcf was applicable for most areas of the plant. An exception was the area of the plant where fiber preparation occurred, where a conversion factor of 7.8 PCM f/cc per mppcf was found. Based on this information, Dement et al. (1983a) concluded that a conversion factor of 3 was appropriate for all operations except preparation, for which a factor of 8 was adopted.

Estimating Cumulative Exposure

Dement et al. (1983a) divided the plant into nine different exposure zones based on similarity of job and exposure characteristics. Within each zone, they identified four different job categories. The concentration in each zone for each job category was estimated from the available exposure data, stratified according to time.

For each worker, the amount of time spent in each exposure zone and each job was derived from work histories compiled from company personnel records (Dement et al. 1983a). These records included information on the plant department and job held by the worker, beginning and ending dates for each job, and dates of absences, termination, and rehire. Exposure duration for the total cohort ranged from 0.1 to 47 years, with a median value of 1.1 years (Hein et al. 2007; Table 1).

Cumulative exposure for each worker was computed by summing the product of concentration *x* time for each exposure zone and job where the worker was employed. Cumulative exposures for individual workers in the total cohort ranged from 0.1 to 700 f/cc-yrs, with a median of 5.5 f/cc-yrs (Hein et al. 2007; Table 1). For analyzing exposure-response relationships for lung cancer mortality, categories of cumulative exposure were selected to give six exposure categories with approximately equal numbers of deaths: <1.5, 1.5-<5, 5-<15, 15-60, 60-<120, and ≥120 f/cc-years (Hein et al. 2007; Table 3). Data for the total cohort were grouped using lag times of 0, 5, or 10 years.

Smoking Data

Smoking information on the cohort is limited. Smoking data were collected from a sample of the cohort in 1964 and 1971 (Dement et al. 1994, Hein et al. 2007). White male smoking prevalence in the cohort (52.4% current smokers, 22.3% past smokers, and 25.3% never smokers) were very similar to U.S. prevalence (51.5% smokers) at the time (Dement et al. 1994). However, for white females in the cohort, smoking prevalence (42.7% smokers, 6.5% past smokers, and 50.8% never smokers) was somewhat higher than U.S. rates (34.2% smokers) (Dement et al. 1994). For non-white males in the cohort, smoking prevalence (38.1% smokers, 14.1% past smokers, 47.8% never smokers) was lower than for U.S. non-white males (60.8% smokers). Because of the differences in smoking prevalence between the cohort and the reference population, calculations of expected lung cancer deaths would tend to be too low for white females and too high for non-white males, which in turn would result in an overestimate of relative risk estimates for lung cancer in white females and an underestimate of relative risks for non-white males.

Lung Cancer Results

Data presented from the most recent study by Hein et al. (2007) were reported based on cumulative exposure, and thus were chosen for use in the OSWER lung cancer model. Analysis of the mortality experience of the cohort through 2001 (compared with U.S. mortality rates) indicated that lung cancer mortality (ICD code 162 (Dement et al. 1994), and identified in Hein et al. (2007) as cancer of trachea, bronchus and lung) was statistically significantly elevated in white males (SMR 2.34; 95%CI 1.94-2.81; 116 observed lung cancer deaths), females (SMR 2.22; 95%CI 1.70-2.85; 61 observed deaths), and all workers combined (SMR = 1.95; 95% CI 1.68-2.24; 198 observed deaths), but was not elevated in non-white males (SMR = 0.85; 95% CI 0.52-1.30; 21 observed deaths) (Hein et al. 2007, Table 2).

Exposure-response relationships were analyzed by grouping the data into six cumulative exposure categories (as noted previously). Life-table analyses (which adjusted for gender, race, age, and calendar year) found statistically significant trends for increasing SMRs with increasing exposure category for the total cohort (grouped with 0, 5, or 10 years of lag), white males, females, and long-term (>1 year of employment) workers, but not for non-white males (Hein et al. 2007, Table 3).

Figure A2-1 shows the number of workers, the person-years at risk (PYAR), and the observed and expected lung cancer deaths for each cumulative exposure group from the Hein et al. (2007) analysis. The authors identified two alternative reasons for the apparent differences in lung cancer risk found between white and non-white males. First, as noted above, the smoking prevalence in non-white males in the cohort was lower than in the reference population, likely leading to an overestimate of expected deaths and an underestimate of relative risk. Second, the authors noted that non-whites tended to be given jobs that dealt with the raw fibers, while whites were generally given jobs dealing with more processed fibers, and that there may have been differences in fiber size distributions between these differing types of operation.

Mesothelioma Results

Three cases of mesothelioma were identified by a manual review of death certificates (Hein et al. 2007). Two occurred in white males with relatively long exposure duration (25 and 32 years) and a long latency (37 and 34 years). An additional case occurred in another white male, nearly 50 years after a relatively short duration of employment (2.5 years) in the mule spinning department. However, data were insufficient for computing mesothelioma incidence as a function of cumulative exposure, so these data can not be employed in the quantitative model fitting effort for this project.

Study by McDonald et al.

Primary: McDonald, A. D., Fry, J. S., Woolley, A. J., and McDonald, J. (1983). Dust exposure and mortality in an American chrysotile textile plant. *British Journal of Industrial Medicine* **40**:361-367.

Other: Sebastian, P., McDonald, J.C., McDonald A.D., Case, B., and Harley, R. 1989. Respiratory cancer in chrysotile textile and mining industries: exposure inferences from lung analysis. Brit. J. Ind. Med. 46:180-187.

Study Description

Cohort Description and Follow-up

McDonald et al. (1983) conducted a retrospective cohort mortality study in the same South Carolina textile plant that was studied by Dement et al. (1982, 1983a, 1983b, 1994). Their cohort consisted of 3,718 men and women employed for at least 1 month before 1959, and for whom a valid social security record existed. The total number of person-years for this cohort is not reported.

Follow-up was begun 20 years from first employment and was carried out through December 31, 1977. The percentage of the workforce lost to follow-up is not reported. On average, men in this cohort began work around age 25 and were employed for 7.5 years. For the analysis, the 1,175 women were excluded. From a total of 2,543 men, 863 (34%) are known to have died.

Determination of Cause of Death and Diagnosis of Lung Cancer/Mesothelioma Cases

Cause of death was determined from the death certificates coded by a single qualified nosologist according to the seventh revision of the International Classification of Diseases (ICD).
Death certificates were obtained for 827 (95%) of the 863 men known to have died.

Reference Population

Expected lung cancer mortality was calculated from rates for South Carolina based on age, gender, race, and year.

Estimating Exposure Concentration

McDonald et al. (1983) had available the same exposure measurements as Dement et al. (1983a). The environmental data were reviewed in detail by an industrial hygienist, considering each operation individually, and noting changes in volume and practices of work, and use of control measures. For each individual worker, estimates of dust concentration in millions of particles per cubic foot (mppcf) were made according to job description year by year.

In their review of the paired and concurrent impinger and filter measurements, McDonald et al. (1983) found particle to fiber conversion factors ranging from 1.3 to 10.0, with an average of about 6 f/cc per mppcf. A value of 6 is intermediate between the values of 3 and 8 found by Dement et al. (1983a) for different areas of the same plant. The value of 6 f/cc per mppcf was used in this report to convert from mppcf to PCM f/cc for this study.

Estimating Cumulative Exposure

Complete employment histories were available for all but five male employees. Each history included age at start of employment, length of gross service, sex, race, and job history. Based on these data, and using the job-specific and time-specific estimates of concentration, McDonald et al. (1983) computed cumulative exposure for each worker expressed in units of mppcf-yrs.

McDonald et al. (1983) describe two practices at the plant that entailed very high exposures. These practices involved the cleaning of burlap bags used in the air filtration system by beating them with buggy whips during the years 1937-1953, and the mixing of fibers, which was carried out between 1945 and 1964 by men with pitch forks and no dust suppression equipment. The authors specifically state that neither they, nor Dement et al. (1983a), gave sufficient weight to these exposures. McDonald et al. (1983) postulate that failure to fully characterize these exposures in their estimates would be unlikely to cause more than a twofold error in accumulated exposure estimates.

Smoking Data

In 1982, the smoking histories of 553 current workers and recent retirees were gathered. Of these, 31% were classified as non-smokers. McDonald et al. (1983) point out that of the 246 men born before 1930, 18% were non-smokers and this latter group may be more representative of the cohort as a whole.

Lung Cancer Results

Lung cancer mortality results for this study were not used in the model fitting effort for this project, because the reports by Dement et al. (1994) and Hein et al. (2007) provide data for this cohort based on longer follow-up periods. However, calculated SMRs for lung cancer mortality in five categories of cumulative exposure (lagged 10 years: <10, 10-<20, 20-<40, 40-<80, and ≥ 80 mppcf-yrs) calculated by McDonald et al. (1983; Figure 2) showed a similar exposure-response relationship as the analyses reported by Dement et al. (1983b).

Mesothelioma Results

McDonald et al. (1983) observed one death from mesothelioma in this cohort. This occurred in a man born in 1904 who worked at the plant for over 30 year and died in 1967 at the age of 63. Necropsy was not performed, although the tumor was stated to be peritoneal. The number of person years of observation were not reported, but may be estimated from total (all-cause) mortality data stratified by age at death, as described in Appendix A, Attachment A-1. Likewise, values of C·Q for each group were not reported, but may be estimated by assuming that the average value of T (time since first exposure) is equal to the midpoint of the age bin minus the average age at first exposure, and combining this with the average value of d (exposure duration) and the average value of C (concentration). These data were combined into one group as described in Attachment A-1 and the resulting values are shown in Figure A2-2.

Uncertainty and Bias Characterization

Appendix C discusses the primary sources of uncertainty in epidemiological studies of cancer risk from asbestos exposure in the workplace and describes the methods used in this document for characterizing the uncertainty. The following sections discuss the uncertainty characterization and issues of potential bias for the lung cancer study of Hein et al. (2007) and the mesothelioma study of McDonald et al (1983).

Uncertainty Due to Measurement Error

As described in Section 3.1 of Appendix C, all estimates of concentration levels of asbestos in the workplace are uncertain due to the combination of sampling error and analytical error. These measurements are usually averaged according to job or work area, often stratified by time. For this cohort, Dement et al. (1983a) report mean concentrations as a function of time period and job category (see Tables IV-XII in the original report). The magnitude of the uncertainty in the reported mean value for each job/time category (which is used to compute cumulative exposure) is a function of a) the number of samples used to compute the mean, b) the between-sample variability, and c) the nature of the underlying distribution. However, the authors do not provide information on the number of samples collected, or on the degree of between-sample variability. Therefore, in the absence of data, the default assumption described in Appendix C is applied to this study to account for measurement error, and is characterized as:

PDF(measurement error) ~ TRI(0.6, 1, 1.5)

Uncertainty in Mean Values for Lung Cancer Exposure Groups

For lung cancer, the point estimate of CE10 is based on the mid-point of the exposure range reported in Table 3 of Hein et al. (2007). In accord with the general approach described in Appendix C, this point estimate is an uncertain estimate of the true mean, and the uncertainty in the point estimate is characterized as follows:

PDF(exposure, bounded) ~ TRI(Min/Mid, 1, Max/Mid)

As discussed in Appendix C, for the highest exposure group that is characterized by an unbounded range (≥ 120 f/cc-yr), the point estimate and uncertainty is modeled as:

PDF(exposure, unbounded) ~ TRI (1, 5/3, 3)

Uncertainty in Conversion Factor (CF) from Dust Data (mppcf) to PCM f/cc

For dust measurements at the South Carolina textile plant, conversion of impinger measurements (mppcf) into units of PCM f/cc was based on data from 120 paired measurements made by midget impinger and PCM collected in 1965, and 986 concurrent samples collected during plant operations from 1968-1971 at the South Carolina textile plant (Dement et al. 1983). Detailed summary statistics on the degree of variability between individual samples are not presented, but the author's state that, for most operations, the mean ratio is between 2.5 and 2.9, and that a value of 3.0 is approximately the upper 95% confidence limit on the ratio. Assuming that the distribution of individual ratios is approximately normal, that the mean is 2.7 and the 95% UCL is 3.0, uncertainty in the site-specific CF may be approximated as follows:

PDF(conversion factor) ~ NORMAL(2.7, 0.18)

Because the authors calculated cumulative exposure using a CF of 3, the uncertainty in the point estimate value of cumulative exposure (CE_{PE}) attributable to uncertainty in the CF may be modeled as:

PDF(conversion factor) ~ NORMAL(2.7, 0.18) / 3 = NORMAL(0.90, 0.06)

However, McDonald et al. (1983) recommended using a CF of 6. Therefore, the uncertainty in the point estimate value of cumulative exposure for the McDonald et al. (1983) study is modeled as:

PDF(conversion factor) ~ NORMAL(2.7, 0.18) / 3 = NORMAL(0.45, 0.03)

Uncertainty Due to Unmeasured Short-Duration High Exposures

As noted above, the authors stated that dust measurements collected in the workplace did not capture short-term but high level exposures that may have occurred during daily "blowing down" and whipping of burlap bags in the dust house. While this almost certainly results in some degree of under-estimation of cumulative exposure for some individuals, it is very difficult to judge a) what fraction of the cohort would have been exposed from this activity, and b) the magnitude of the error in cumulative exposure that might result. For example, if the job was always performed by the same individuals, their cumulative exposures would be substantially underestimated, but the person-years of observation for these individuals would constitute only a small fraction of the total observations. Conversely, if the job was rotated among many individuals, then the magnitude of the error in the cumulative exposure for each person-year would be small, and would likely result in only a small number of person years being re-classified from one exposure bin to the next highest bin. In the absence of data, and recognizing that the authors of the study did not attempt to adjust for these exposures, no added uncertainty is added in this analysis to account for this underestimation. Note that failure to account for underestimation of exposure, if significant, would tend to result in an overestimation of potency.

Uncertainty in the Use of Stationary Rather Than Personal Air Monitors

For this plant, measures of asbestos in air were based on stationary monitors placed at various locations around the factory. As discussed in Appendix C, use of stationary monitors may tend to underestimate the true exposure level of workers, especially those engaged in activities that actively disturb asbestos-containing materials or dusts. Based on available data (Table C-2) on the ratio of particulate concentrations measured using personal to stationary monitors at various locations, the uncertainty attributable to this source may be characterized as:

PDF(personal vs. stationary) ~ BETA(2, 20, 0.9, 10)

Uncertainty in Temporal Representativeness

For the South Carolina textile plant, dust and/or PCM measurements are available from 1930 forward. The cohort being evaluated by Hein et al. (2007) was exposed from 1940 to 1965, and the cohort evaluated by McDonald et al. (1983) was exposed from 1938 to 1958. Thus, for both studies, data on concentration levels are available over the duration of the study period. Based on this, uncertainty in temporal representativeness is ranked as low, and is characterized by:

PDF(temporal representativeness) ~ TRI(0.9, 1, 1.1)

Bias Correction Factor in Lung Cancer Data Reported as CE Rather Than CE10

Hein et al. (2007) report lung cancer mortality by cumulative exposure with no lag, with a five-year lag, and with a 10-year lag. The data that incorporated a 10-year lag were used in this evaluation. Therefore, no BCF is required for this cohort.

Uncertainty in Mesothelioma Data

As discussed in Attachment 1, two approximations were necessary in order to utilize the data from the study by McDonald et al. (1983) in the quantitative mesothelioma model fitting exercise. First, it was necessary to estimate the number of person-years of observation from all-cause mortality data, and second, it was necessary to estimate the value of cumulative exposure (C·Q) from data on the average age at first exposure, the average exposure duration, and the average exposure concentration. As described in Attachment 1, the combined uncertainty associated with these approximations may be characterized as follows:

PDF(combined effect of approximations) ~ TRI (0.4, 1, 2.5)

Uncertainty in Fraction Amphibole

The workers at the South Carolina textile plant were primarily exposed to chrysotile asbestos. Although a small amount of crocidolite was used in the manufacture of braided packing and tape starting in the 1950s, the amount used was essentially negligible compared to the amount of chrysotile, and in addition, releases from the crocidolite would have been expected to be minor. However, as discussed in Appendix C, nearly all commercial chrysotile contains low level amphibole contamination. Sebastien et al. (1989) examined lung samples taken at autopsy from deceased workers and identified the presence of five asbestos types, including chrysotile, tremolite, amosite, crocidolite, and talc-anthophyllite. The results are summarized below:

Mineral type	Chrysotile	Tremolite	Amosite + crocidolite	Talc-anthophyllite
Geomean (number/ug)	0.63	0.38	0.14	0.11

Although these data are not sufficient to estimate the value of f_{amph} in inhaled workplace air, the data do support the conclusion that f_{amph} is not zero. Therefore, as discussed in Appendix C, in the absence of any site-specific data from TEM analyses of workplace air, uncertainty in f_{amph} is characterized as:

$$PDF(f_{amph}) \sim LN(0.00054, 0.001)$$

Uncertainty in Particle Size Data for Chrysotile

For this study, the primary type of asbestos used at the textile plant was chrysotile. Of the TEM data sets available (see Appendix B), three are derived from samples collected within the textile industry. These data sets differ by operation (preparation, twisting, and weaving). All of these operations were performed at the South Carolina plant, and as the mortality data is not reported by operation, the three data sets are combined to represent the whole plant. Since the TEM data are based on chrysotile asbestos collected within the same industry, the uncertainty around f_{size} (chrysotile) is ranked as low and is characterized by:

$$PDF(f_{size[chrysotile]}) \sim TRI(0.9, 1, 1.1)$$

Uncertainty in Particle Size Data for Amphibole

Of the TEM data sets available (see Appendix B), 18 are based on amphibole asbestos, but none are based on samples from the textile industry. As mentioned above, crocidolite yarn was used at the South Carolina factory, but this is considered to be negligible. As discussed in Appendix C, chrysotile asbestos tends to contain trace amounts of amphibole contamination, generally characterized as tremolite. Therefore, the one TEM data sets based on tremolite in the mining industry was applied to this study. In accord with the general approach described in Appendix C, when the TEM data set matches on amphibole type but not industry, uncertainty is ranked as medium and is characterized by:

$$PDF(f_{size[amphibole]}) \sim TRI(0.5, 1, 1.5)$$

Figure A2-1. Lung Cancer Mortality in South Carolina Textile Workers as a Function of Cumulative Exposure with a 10-Year Lag (CE10) (Data Source: Hein et al. 2007).

CE10 (PCM f/cc-yr)			Number of Workers	Number of PYAR	Mortality		
Min	Max	Mid			Obs	Exp	RR
0	1.5	0.75	705	26667	34	22.1	1.5
1.5	5	3.25	756	29188	33	25.3	1.3
5	15	10	628	24449	34	21.7	1.6
15	60	37.5	524	20561	35	18.8	1.9
60	120	90	264	10295	37	9.2	4.0
120		200	195	7352	25	4.7	5.4

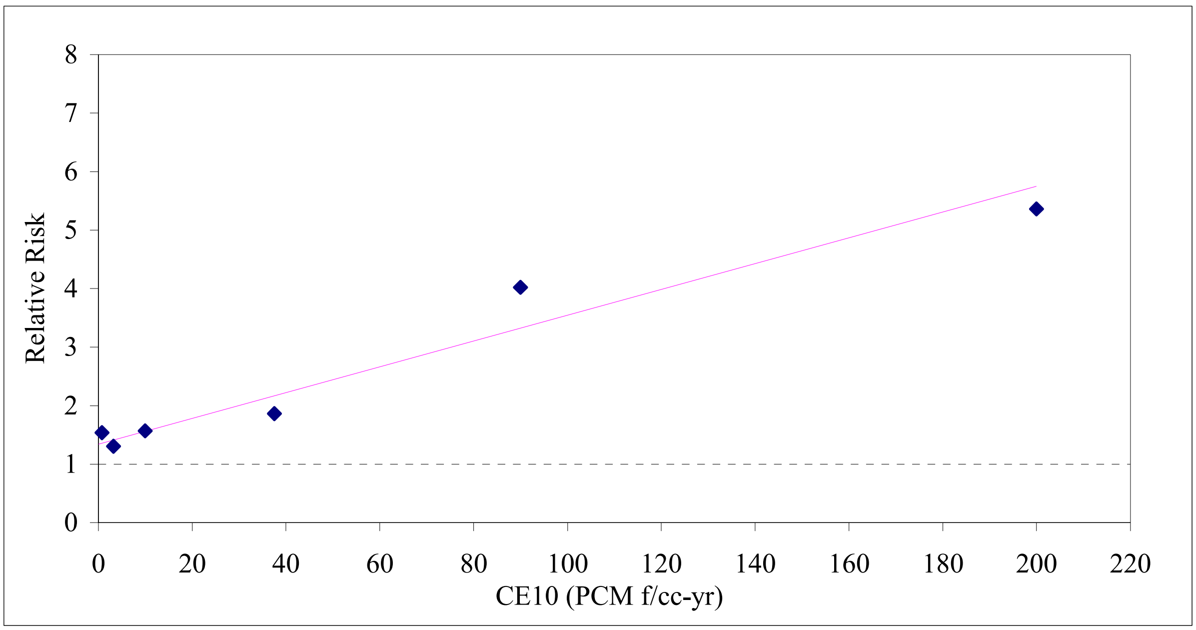


Figure A2-2. Mesothelioma Data for South Carolina Textile Workers (Data Source: McDonald et al. 1983).

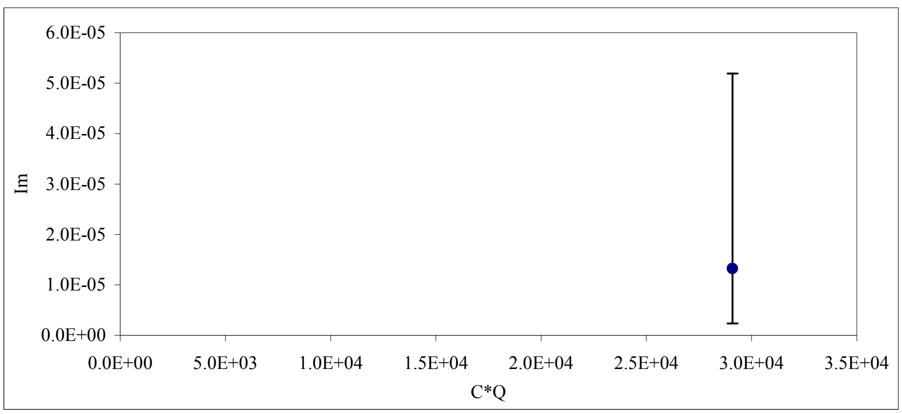
Age at Death		Avg Age at Start (a)	Yrs since start	D (yrs) (a)	Q (yrs^3)	Conc (a,b)		Reconstruction of PY (c)		
Range	Pt. Est.					mppcf	f/cc	Observed Deaths (d)	SMR (e)	PY
26-44	34.9	25.77	9.12	7.59	0	1.80	10.80	178	1.274	46173
45-64	54.5	25.77	28.73	7.59	5188	1.80	10.80	502	1.274	26914
>= 65	75.0	25.77	49.23	7.59	28700	1.80	10.80	177	1.274	2203

a) Observed values reported in Table 3 (McDonald et al. 1983).
b) Dust concentrations were measured by impinger. An assumed conversion factor of 6 was applied to convert to PCM (f/cc).
c) Person-years were reconstructed based on the method presented in Attachment A-1.
d) Observed deaths from all causes for the given age groups are reported in Table 1 (McDonald et al. 1983).

e) SMR for all cause deaths for the complete cohort reported in Table 4 (McDonald et al. 1983). The same value is assumed to apply to all groups.

C*Q (f)	PY (g)	Observed Cases	Incidence (Im)	Uncertainty Bounds	
				5% LB	95% UB
29098	75289	1	1.33E-05	2.3E-06	5.2E-05

f) Calculated as the P- weighted average as described in Appendix C.
g) Calculated as the sum of the reconstructed PY across all three age bins.



A3. Retirees from a U.S. Asbestos Products Company

References

Primary: Enterline, P. E., Hartley, J. and Henderson, V. (1987). Asbestos and cancer: a cohort followed up to death. *British Journal of Industrial Medicine*, **44**: 396-401.

Henderson, V. and Enterline, P. E. (1979). Asbestos exposure: factors associated with excess cancer and respiratory disease mortality. *Annals of the New York Academy of Sciences*, **330**: 117-126.

Other: Enterline, P. E. and Henderson, V. (1973). Type of asbestos and respiratory cancer in the asbestos industry. *Archives of Environmental Health*, **27**: 312-317.

Enterline, P.E. (1965). Mortality among asbestos products workers in the United States. *Annals of the New York Academy of Sciences*, **132**(1): 156-165.

Study Description

Location and Facility Description

The company, the largest producer of asbestos products in the United States, has production facilities at multiple locations. The company manufactured a range of different types of asbestos-containing products, including asbestos cement shingles and sheets, insulation materials, textiles, friction products, and asbestos cement pipe. Further details on the processes and production are not provided.

Asbestos Type

The types of asbestos used at various facilities operated by this company included amosite, chrysotile, and crocidolite. The types used varied by department, depending on the products manufactured. Although quantitative data are limited, the authors stated that crocidolite and chrysotile were used in manufacturing cement pipe, and crocidolite comprised 3-5% of the final product. Workers involved with the manufacturing of asbestos cement shingles and sheets were exposed only to chrysotile asbestos. Amosite was used in cement pipes and other products.

Fraction Amphibole

As reported above, the types of asbestos that were used differed between operations. As discussed below, the authors presented mortality data for workers stratified according to the types of asbestos they were exposed to, as follows:

1. Amosite only
2. Chrysotile only
3. Chrysotile and crocidolite in cement pipe
4. Chrysotile and crocidolite in other products
5. Amosite, chrysotile, and crocidolite in cement pipe
6. Amosite, chrysotile, and crocidolite in other products

As discussed in Appendix C, amphibole asbestos is not known to be contaminated with chrysotile , so f_{amph} is assumed to be approximately 100% for group 1. For group 2, because chrysotile is believed to be contaminated with trace levels of amphibole, f_{amph} is assumed to be 0.054%. For group 3, it was reported that crocidolite comprised 3-5% of the final product of asbestos cement pipe, and the Ontario Royal Commission (1984) reported that crocidolite constitutes approximately 20% of the asbestos used in the pipe process (Ontario Royal Commission, 1984). On this basis, f_{amph} for group 3 is assumed to be 20%. For group 4, no information is available on the nature of the products or the fraction amphibole, so this group was not retained for evaluation. For group 5, no data on the percentage of amosite used was reported, but it is assumed that the ratio of amphibole to chrysotile in cement pipe is likely to remain at about 20%. Therefore f_{amph} for group 5 was assumed to be 20%. For group 6, like group 4, no data are available on the relative amounts of amphibole and chrysotile used, so this group was not retained for evaluation. In summary, the following groups were retained, with estimated f_{amph} fractions as shown:

Amosite only (group 1)	f_{amph} = 100%
Chrysotile only (group 2)	f_{amph} = 0.054%
Cement pipe workers (groups 3 and 5) (chrysotile, amosite and crocidolite)	f_{amph} = 20%

Cohort Description and Follow-up

The total cohort consisted of men who retired from the company during the years 1941-1967 and who completed their working lifetime as production or maintenance employees of the company. The cohort included three groups of men: those who retired normally at the age of 65, those who retired before the age of 65 because of personal reasons, and those who retired before the age of 65 because of a disability. A total of 1,075 males were included. The total number of person-years included in the cohort was not reported. The average duration of employment in the asbestos industry was 25 years (range 3-51 years) (Henderson and Enterline 1979).

One potential limitation of this study is that, because the cohort consisted only of men who retired from the company, a "healthy worker effect" may tend to confound the results. In addition, the data do not include the mortality experience of individuals who died or left employment before retirement. This is a significant limitation to the data.

As noted above, because the asbestos atmosphere varied between different parts of the factory, the authors stratified the cohort according to the type of asbestos exposure that occurred. The size of these sub-cohorts are as follows:

Group	Asbestos Type	Number of men
1	Amosite only	58
2	Chrysotile only	754
3	Chrysotile and crodicolite in cement pipe	98
4	Chrysotile and crodicolite in other products	83
5	Amosite, chrysotile, and crocidolite in cement pipe	29
6	Amosite, chrysotile, and crocidolite in other products	14
7	Other	39

Follow-up by Henderson and Enterline (1979) was carried out through 1973. During this period, 781 deaths were reported among the 1,075 male workers included in the cohort. Enterline et al. (1987) extended this follow-up period through 1980, whereby an additional 162 deaths were recorded. These follow-up data were not included in the lung cancer data set used in the current fitting effort because mortality was presented for the entire cohort and was not stratified according to asbestos type.

Determination of Cause of Death and Diagnosis of Lung Cancer/Mesothelioma Cases

By the end of follow-up in 1973, 73% of this cohort was deceased. Cause of death was ascertained from death certificates coded by a qualified nosologist according to the seventh revision of the International Classification of Diseases (ICD). Only 18 death certificates could not be located for the 782 reported deaths.

Reference Population

Expected deaths were calculated using mortality rates for the entire U.S. white male population living at the same ages and time periods of the retirees. These death rates were coded under the fifth, sixth, or eighth revision of the ICD. Henderson and Enterline (1979) used comparability ratios to translate expected mortality to the seventh revision. The calculation of the expected number of deaths followed the modified life table method (Enterline 1965).

Estimating Exposure Concentration

Environmental hygiene surveys started in the mid-1950s were used to estimate dust measurements in million particles per cubic foot (mppcf). For earlier periods, dust levels were estimated by the company industrial hygienist based on knowledge of past plant operations and conditions. Jobs were assigned to one of six classes or ranges based on rough classification as often times there was not enough information to estimate the dust level for each job. The six classes were defined as: no exposure (0), less than 5 mppcf (2.5), 5-10 mppcf (7.5), 10-30 mppcf (20), 30-50 mppcf (40), and 50 or more mppcf (62.5). No site-specific data are available for conversion from mppcf to PCM f/cc. Therefore, as discussed in Appendix C, a default factor of 3 PCM f/cc per mppcf was used for the calculations presented in this report.

Estimating Cumulative Exposure

Cumulative exposure estimates at the time of retirement were made for each worker using information from personnel records and taking into consideration process changes, machine installations, ventilation controls, and judgmental determinations, as made by the authors. For each man, the dust level based on job description and time period worked was multiplied by the duration of exposure and summed across all jobs during his working lifetime.

Smoking Data

Henderson and Enterline (1979) do not report on the smoking prevalence of the U.S. retirees.

Lung Cancer Results

As described above, for the purposes of this assessment, this cohort was divided into three sub-groups: 1) workers exposed to amosite only, 2) workers exposed to chrysotile only, and 3) workers exposed to a mixture of amosite, chrysotile and crocidolite in the pipe process. Raw mortality data based on respiratory cancer (ICD not reported) derived from Table 4 in Henderson and Enterline (1979) are presented in Figures A3-1, A3-2, and A3-3. Since the data for each sub-cohort are not stratified according to cumulative exposure but are reported only as a single group, a baseline risk (α) cannot be estimated from these data alone. However, Enterline et al. (1987) provide data that allow calculation of the value of α of 1.43 for the combined cohort (see Figure A3-4). Assuming that there are no substantial differences in the baseline risk of lung cancer as a function of the type of asbestos exposure that occurred, this value of α can be applied to each of the sub-cohorts, allowing the retention of the data from this study for use in the fitting effort for lung cancer.

As seen, all three groups had SMR values that were statistically higher than one. The highest SMR (579) was for workers exposed to chrysotile and crocidolite in the pipe manufacturing process.

Mesothelioma Results

Henderson and Enterline (1979) evaluated 479 retired male production or maintenance service workers during the updated follow-up period from 1970-1973. These men were alive at the end of 1969 and had celebrated their 65th birthday prior to 1968. Three recorded mesotheliomas were reported. These authors also report two mesothelioma deaths that occurred within the cohort prior to 1970. In the follow-up report, Enterline et al. (1987) reported the occurrence of eight deaths from mesothelioma, two of which were peritoneal. Asbestos exposures were reported for these eight cases, with values ranging from 48 to 760 mppcf-yr (about 150 to 2300 f/cc-yrs). These exposures are relatively low compared to other members of the cohort. Six of the eight men were stated to have been exposed primarily to chrysotile, while two were exposed to amosite or crocidolite. However, neither of these studies presented data on mesothelioma incidence as a function of cumulative exposure ($C \cdot Q$), so these observation can not be included in the quantitative mesothelioma exposure-response model.

Uncertainty and Bias Characterization

Appendix C discusses the primary sources of uncertainty in epidemiological studies of cancer risk from asbestos exposure in the workplace and describes the methods used in this document for characterizing the uncertainty. The following sections discuss the uncertainty characterization and issues of potential bias for this study.

Uncertainty Due to Measurement Error

As described in Section 3.1 of Appendix C, all estimates of concentration levels of asbestos in the workplace are uncertain due to the combination of sampling error and analytical error. These measurements are usually averaged according to job or work area, often stratified by time. For this study, Henderson and Enterline (1979) categorized jobs in to six concentration ranges as described above. The magnitude of the uncertainty in the reported mean value for each job/time category (which is used to compute cumulative exposure) is a function of a) the number of samples used to compute the mean, b) the between-sample variability, and c) the nature of the underlying distribution. However, the authors do not provide information on the number of samples collected, or on the degree of between-sample variability. Therefore, in the absence of data, the default assumption described in Appendix C is applied to this study to account for measurement error, and is characterized as:

PDF(measurement error) ~ TRI(0.6, 1, 1.5)

Uncertainty in Mean Values for Exposure Groups

The lung cancer mortality data reported by Henderson and Enterline (1979) are reported according to mean cumulative exposures. Therefore, no uncertainty distribution is needed for this factor.

Uncertainty in Conversion Factor (CF) from Dust Data (mppcf) to PCM f/cc

Workplace dust measurements were obtained from environmental hygiene surveys that started in the 1950's. All measurements were made using midget impingers. No site-specific conversion factor for this company is available. Therefore, as discussed in Appendix C, in the absence of data, a default conversion factor of 3.0 is assumed, with the following uncertainty distribution:

PDF(conversion factor) ~ TRI(0.33, 1, 3.33)

Uncertainty in the Use of Stationary Rather Than Personal Air Monitors

Measures of asbestos in air at this company are based on stationary area monitors. As described in Appendix C, the use of stationary air monitors tends to underestimate exposures compared to personal monitors. Based on this, the uncertainty in cumulative exposure due to the use of stationary area monitors is characterized as:

PDF(personal vs. stationary) ~ BETA(2,20,0.9,10)

Uncertainty in Temporal Representativeness

Routine sampling of the workplace environments did not begin until the mid-1950's. Conditions prior to this period were extrapolated by a company hygienist. The cohort is defined as men who retired from service during 1941- 1967. Therefore, most workers were exposed, at least in part, prior to the start of environmental monitoring. As discussed in Appendix C, when data are available for only a limited time interval of the exposure period, and the use of extrapolated data is predominate, the uncertainty is considered to be high and is characterized as follows:

PDF(temporal representativeness) ~ TRI(0.5, 1, 1.5)

Bias Correction Factor in Data Reported as CE Rather Than CE10

This study reports cumulative exposure as CE rather than as CE10. As discussed in Appendix C, use of CE rather than CE10 introduces a potential bias that depends on the average duration and level of exposure, the average length of time of follow-up since last exposure, and whether or not a minimum latency was used in forming the dose groups. Henderson and Enterline (1979) report an average duration of 25 years. End of follow-up was 1973 and the average time since last exposure was estimated to be 19 years. Data are stratified by person (rather than person-year). Based on this information, a BCF was assigned to each of the U.S. retiree cohorts as follows:

BCF ~ TRI(1.3, 1.4, 1.6)

Uncertainty in Fraction Amphibole

As noted above, three cohorts were used in the fitting effort, stratified based on the type of amphibole used in the workplace:

- Cohort 1 = Workers exposed to amosite asbestos only. As discussed in Appendix C, because no data were located to suggest that amphibole asbestos is contaminated with chrysotile, the fraction amphibole is assumed to be equal to 100% for this cohort.

- Cohort 2 = Workers exposed to chrysotile asbestos only. As discussed in Appendix C, available data suggest that chrysotile may contain trace levels of amphibole contamination, so uncertainty around f_{amph} for this cohort is modeled as:

  $$PDF(f_{amph}) \sim LN(0.00054, 0.001)$$

- Cohort 3 = Workers in the pipe section were exposed to chrysotile plus amphibole (crocidolite and amosite). Based on the Ontario Royal Commission, (1984), the fraction of amphibole used in pipe production is about 20%, but the variability in this fraction is not discussed. In the absence of any additional information, the uncertainty bounds around this point estimate are characterized as follows::

  $$PDF(f_{amph}) \sim TRI(0.15, 0.20, 0.25)$$

Uncertainty in Particle Size Data for Chrysotile

Cohort 1 (amosite only). Workers in cohort 1 were reported to have only been exposed to amosite asbestos. An uncertainty distribution around f_{size} (chrysotile) is not necessary.

Cohort 2 (chrysotile only). Workers in cohort 2 were reported to have only been exposed to chrysotile asbestos. Of the TEM data sets available (see Appendix B), 11 are based on chrysotile asbestos. For this study, it is known that the chrysotile was used in a range of different products and processes, so there is no strong basis for preferring any one chrysotile TEM data set over any other. Therefore, all chrysotile TEM data sets were combined by averaging across the data sets within each specified size bin. In accord with the general approach described in Appendix C, the uncertainty in a mixed industry data set is ranked as medium and is characterized by:

$$PDF(f_{size[chrysotile]}) \sim TRI(0.5, 1, 1.5)$$

Cohort 3 (mixed exposure – pipe process). Workers in cohort 3 were reported to have been exposed to chrysotile, crocidolite, and some amosite. Of the TEM data sets available (see Appendix B), 11 are based on chrysotile asbestos. Three of these are from plants manufacturing asbestos-cement pipe. These data sets differ by operation as mixing, forming, and finishing. Since the mortality data was not presented categorized by operation, these three chrysotile data sets were combined by averaging the size bins across operations to represent the particle size distribution for chrysotile exposures for Cohort 3. In accord with Appendix C, uncertainty is rated as low and is represented by:

$$PDF(f_{size[chrysotile]}) \sim TRI(0.8, 1, 1.2)$$

Uncertainty in Particle Size Data for Amphibole

<u>Cohort 1 (amosite only)</u>. Workers in cohort 1 were exposed only to amosite asbestos. Based on the report, it appears that amosite was used in some cement pipe production, but was also used in other (unspecified) operations. Of the 18 TEM data sets for amphibole asbestos, 5 are based on amosite, based on mining/milling and insulation manufacturing. These five amosite data sets were combined to represent the particle size distribution for amphibole exposures for Cohort 1. In accord with the table above, uncertainty is rated as medium and is represented by:

$$PDF(f_{size[amphibole]}) \sim TRI(0.5, 1, 1.5)$$

<u>Cohort 2 (chrysotile only)</u>. Workers in cohort 2 were reported to have only been exposed to chrysotile asbestos. However, as described in Appendix C, tremolite may occur as a trace contaminant in chrysotile asbestos. There is only one TEM data set for tremolite asbestos, based on the mining/milling industry. In accord with the general approach described in Appendix C, in this case uncertainty in the particle size data is ranked as medium and is characterized by:

$$PDF(f_{size[amphibole]}) \sim TRI(0.5, 1, 1.5)$$

<u>Cohort 3 (mixed exposure – pipe process)</u>. Workers employed in the pipe production process of this company were exposed to crocidolite asbestos, and to a lesser degree amosite asbestos. The authors only discussed crocidolite exposure, and for the most part it is assumed that amosite exposure in the pipe process is negligible. Of the 18 TEM data sets for amphibole asbestos, three are based on crocidolite asbestos in plants manufacturing asbestos-cement pipe. These data sets were combined by averaging the size bins across operations to represent the particle size distribution for amphibole exposures for Cohort 3. In accord with the general approach described in Appendix C, uncertainty is ranked as low and is represented by:

$$PDF(f_{size[amphibole]}) \sim TRI(0.8, 1, 1.2)$$

Figure A3-1. Raw Lung Cancer Data for U.S. Retirees Exposed to Amosite Only

CE (mppcf-yr) Mean (a)	CE (PCM f/cc-yr) Mean (b)	Observed Deaths (a)	Expected Deaths (c)	SMR (a)	Relative Risk		
					Pt. Est. (d)	5% LB	95% UB
330	990	4	1.1	363.6	3.6	1.5	7.7

a) Data reported in Table 4 (Henderson and Enterline 1979)

b) A site-specific conversion factor is not available for this cohort; assume the default conversion factor of 3.0 for the range of conversion factors observed among available studies (see Appendix C for further explanation).

c) Calculated value (observed deaths/relative risk)

d) Relative risk equal to SMR/100

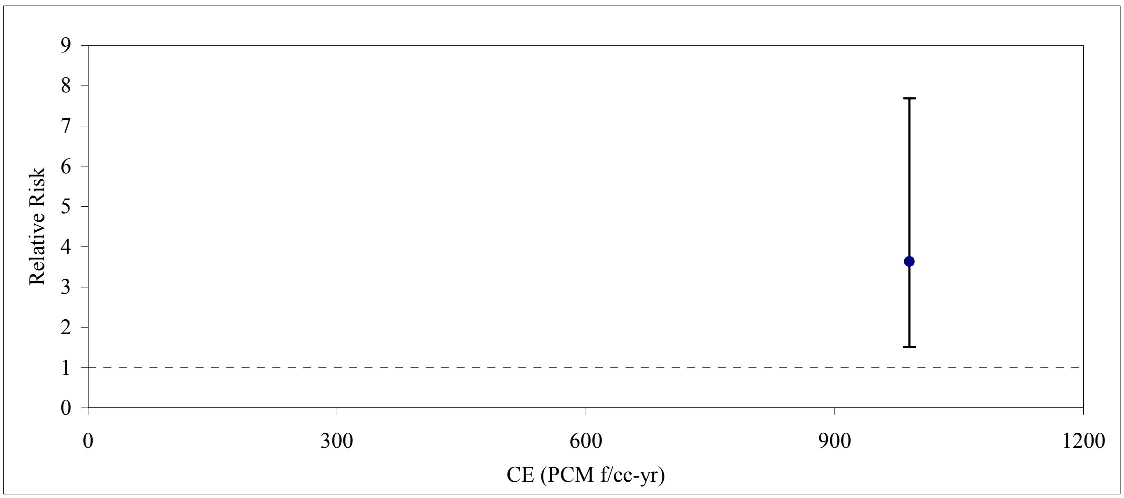


Figure A3-2. Raw Lung Cancer Data for U.S. Retirees Exposed to Chrysotile Only

CE (mppcf-yr)	CE (PCM f/cc-yr)	Observed	Expected		Relative Risk		
Mean (a)	Mean (b)	Deaths (a)	Deaths (c)	SMR (a)	Pt. Est. (d)	5% LB	95% UB
244	732	40	16.2	246.9	2.5	1.9	3.2

a) Reported in Table 3 (Henderson and Enterline 1979)

b) A site-specific conversion factor is not available for this cohort; assume the default conversion factor of 3.0 for the range of conversion factors observed among available studies (see Appendix C for further explanation).

c) Calculated value (observed deaths/relative risk)

d) Relative risk equal to SMR/100

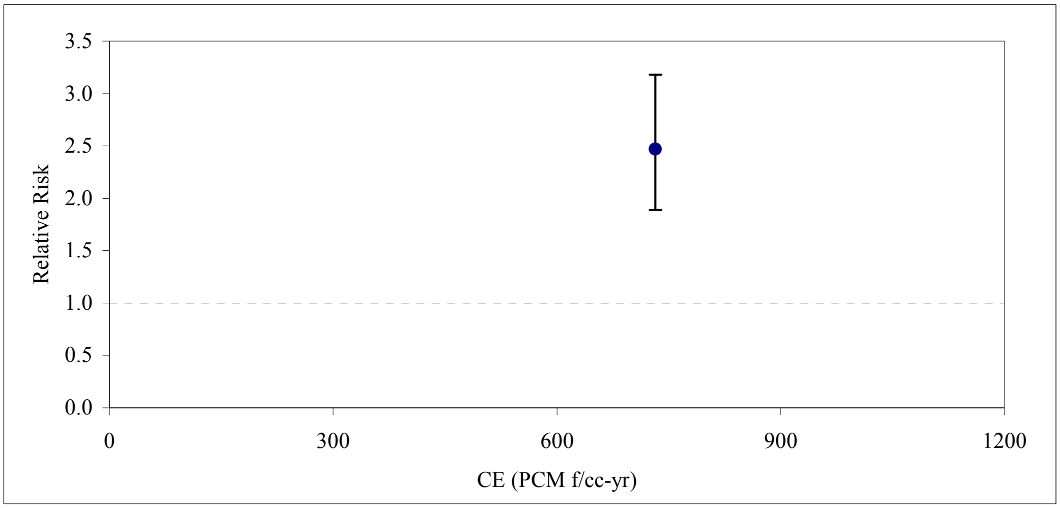


Figure A3-3. Raw Lung Cancer Data for U.S. Retirees Exposed to a Mixed Atmosphere During the Manufacturing of Asbestos Cement Pipe

CE (mppcf-yr) Mean (a)	CE (PCM f/cc-yr) Mean (b)	Observed Deaths (c)	Expected Deaths (d)	Relative Risk		
				Pt. Est. (d)	5% LB	95% UB
230	690	12	2.3	5.2	3.2	8.2

a) Weighted average of mean exposures for the two groups of cement pipe workers reported in Table 4 (Henderson and Enterline 1979)

b) A site-specific conversion factor is not available for this cohort; assume the default conversion factor of 3.0 for the range of conversion factors observed among available studies (see Appendix C for further explanation).

c) Sum of observed deaths reported in Table 4 (Henderson and Enterline 1979)

d) Expected deaths calculated as the sum of the expected deaths calculated from reported data in table 4 (Henderson and Enterline 1979) on observed deaths and SMR (observed deaths/(SMR*0.01)) for each of the two groups of cement pipe workers.

e) Relative risk calculated as observed deaths/expected deaths.

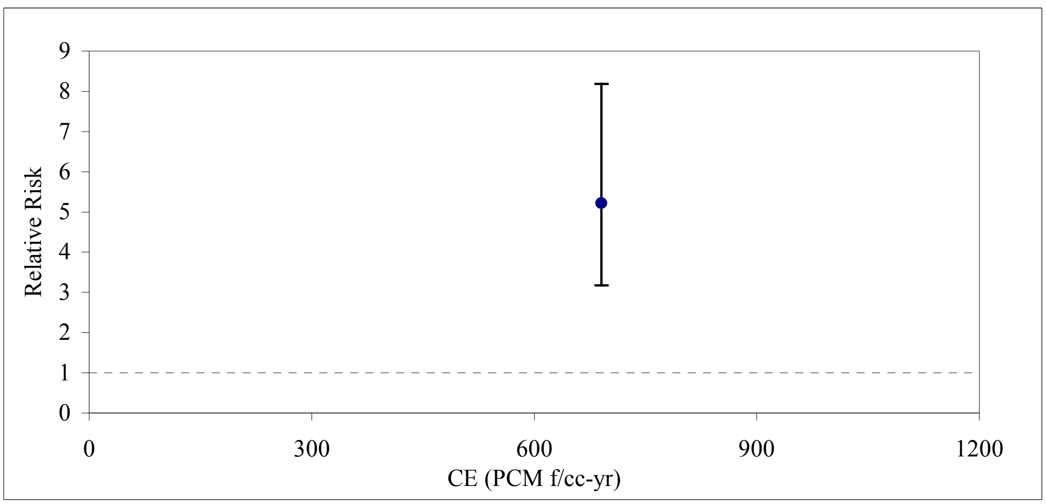


Figure A3-4. Raw Lung Cancer Data for U.S. Retirees Based on Enterline et al. (1987)

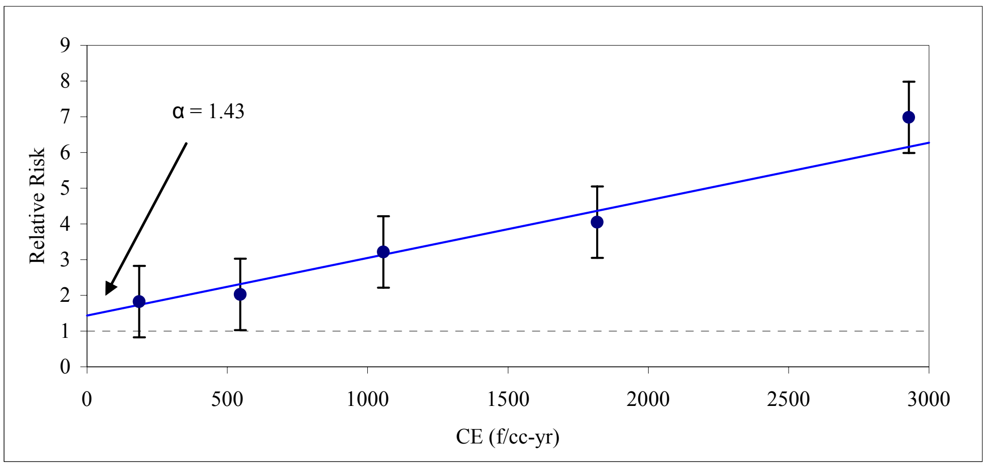
CE (mppcf-yr)		CE (PCM s/cc-yr)	Observed	Expected	Relative Risk		
Range (a)	Mean (a)	Mean (b)	Deaths (a)	Deaths (c)	Pt. Est. (d)	5% LB	95% UB
<125	62	186	23	12.6	1.8	1.3	2.5
125-249	182	546	14	6.9	2.0	1.3	3.1
250-499	352	1056	24	7.5	3.2	2.3	4.5
500-749	606	1818	10	2.5	4.1	2.3	6.6
>=750	976	2928	8	1.1	7.0	3.8	12.0

a) Data reported in Table 4 (Enterline et al. 1987)

b) A site-specific conversion factor is not available for this cohort; assume the default conversion factor of 3.0 for the range of conversion factors observed among available studies (see Appendix C for further explanation).

c) Calculated value (observed deaths/relative risk)

d) Relative risk equal to SMR/100



A4. Ontario Cement Manufacturing Plant

References

Primary: Finkelstein, M. (1984). Mortality among employees of an Ontario asbestos-cement factory. *American Review of Respiratory Disease,* **129**:754-761.

Other: Finkelstein, M. (1983). Mortality among long-term employees of an Ontario asbestos-cement factory. *British Journal of Industrial Medicine* **40**:138:144.

Ontario Royal Commission. 1984. Report of the Royal Commission on Matters of Health: Safety Arising from the use of Asbestos in Ontario. Volume 3.

CHAP. 1983. Chronic Hazard Advisory Panel on Asbestos. Report to the U.S. Consumer Products safety Commission. July 1983.

Study Description

Location and Facility Description

The factory is located in Ontario, Canada. Production began in 1948 with the manufacturing of asbestos cement pipe and rock-wool insulation in separate buildings. From 1955-1970, asbestos cement board was produced in a third building. Starting in 1960, asbestos insulation materials were manufactured in this same building.

Asbestos Type

Both chrysotile and crocidolite were used in production of cement pipe, but only chrysotile was used in the cement board operation. No further information is available regarding the type of asbestos used in the production of asbestos insulation materials. The Ontario Royal Commission reports that crocidolite constitutes approximately 20% of the asbestos used in the pipe process (Ontario Royal Commission, 1984).

Fraction Amphibole

As noted above, the fraction amphibole differs between the two asbestos-product buildings at this plant, with a value of about 20% for the pipe production building (20% crocidolite, 80% chrysotile) and a value of approximately zero for the cement board area (approximately pure chrysotile). The study description does not reveal whether workers at this plant tended to be exposed primarily in one area or the other, or whether workers tended to move between buildings. Because the author chose not to stratify the data, it is assumed that most workers were exposed in both buildings. In the absence of any additional data, it is assumed that the time spent in each building was 50% of the total. Thus, the point estimate for fraction amphibole is about 10%.

Cohort Description and Follow-up

The cohort consisted of employees with a minimum of one year of employment that had been hired before 1960. This group consisted of 535 men divided among three sub-groups: production workers exposed to asbestos dust for at least one month prior to the end of 1961 in the pipe or board shops, maintenance workers, and men employed in the rock wool/fiber glass operations who were only exposed minimally to asbestos dust only after 1961. An additional 205 employees were identified as factory control subjects (non-exposed) for internal comparison.

Follow-up occurred in two stages. The first continued until 1977 using data provided by the Canadian Mortality Data Base at Statistics Canada. The second involved a search of the Ontario Death Registry through 1981 for men with Ontario addresses. Through this search, 16% of the cohort were found to be alive, but could not be located. Based on the assumption that these men would be similar to those who could be located during the first stage of follow-up, they were withdrawn from the mortality analysis at the end of 1977.

Determination of Cause of Death and Diagnosis of Lung Cancer/Mesothelioma Cases

Cause of death was determined from death certificates which were available for all but one death. For this case, the cause of death was obtained from family members. In addition, available reports on pathology and autopsy were obtained where available. . An internal comparison was also conducted based on “best evidence” classification of the causes of death among the production workers.

Reference Population

Expected deaths were calculated from Ontario mortality rates.

Estimating Exposure Concentration

Impinger area sampling was performed in 1949, 1954, 1955, 1957, and semi-annually during the 1960s. Personal PCM membrane sampling began in late 1969. Exposures were assumed to have been the same from 1962 to 1970, to have been 30% higher from 1955 to 1961, and to have been twice as high from 1948 to 1954. Finkelstein (1984) judged that the resulting exposure estimates were "accurate to within a factor of three or five." No site-specific conversion factor was reported by the authors for this factory.

Estimating Cumulative Exposure

Cumulative exposure estimates were made through the use of employment records maintained by the company. The records contained details on the job assignments of each employee. Exposures of maintenance workers were not estimated, and the exposure response analysis consequently involved only the unexposed “factory control” workers (N=205) and the production workers (N=428). Estimates for jobs where baseline measurements from 1969 to 1970 were unavailable were based on a combination of measurements from other jobs.

Smoking Data

Smoking histories were available for 17 of the 23 lung cancer cases. All but one were current or former smokers. Data on smoking incidence in the cohort as whole were not reported.

Lung Cancer Results

Table 7 in Finkelstein (1984) presents data on lung cancer incidence in this cohort (ICD 162 which according to ICD-7. Data are reported as incidence rates (cases per 1,000 man-years), stratified according to five cumulative exposure bins. There was a statistically significant upward trend in lung cancer death rates as a function of cumulative exposure ($p < 0.01$).

Data on lung cancer mortality rates from Table 7 of Finkelstein (1984) were converted to estimates of relative risk by dividing by the lung cancer mortality rate in Ontario males

(1.3 cases per 1,000 man-years). The rate for unexposed "factory control" workers was not used because this rate was based on only 3 deaths.

The resulting values are presented in Figure A4-1. As seen, there is an apparent increasing exposure-response trend except for the highest exposure group. When all groups are considered, there is no clear trend. Finkelstein (1984) speculated that the reason lung cancer mortality did not increase steadily with exposure, may be due to competing causes of death. In this regard the only example that the authors present is that 53% of the deaths observed were due to mesothelioma or gastrointestinal cancer.

Mesothelioma Results

There were 21 mesothelioma deaths in the cohort, 19 of which had pathologic review. Based on a "best evidence" classification of cause of death, Finkelstein (1984) identified 17 deaths from mesothelioma among production workers. Five additional deaths from mesothelioma occurred among former employees who had under nine years of employment and thus were not included in the analysis. One man reported to have died from peritoneal mesothelioma had no recorded employment in an asbestos area at the plant.

Table 3 of Finkelstein (1984) presents the 17 mesothelioma deaths based on "best evidence" categorized by years since first exposure. This table also provides the mortality rate, from which can be calculated the person-years of observation. Finkelstein (1984) states that the average cumulative exposure for production workers was about 60 f-y/ml, but does not provide information for determining duration and level of exposure separately. CHAP (1983) used an average exposure of 9 f/cc for a sub-cohort of production workers, although they provided no support for this assumption. If this value is assumed to be appropriate for the expanded cohort, the average duration is estimated as about 60/9 = 6.7 years. Based on this, the value of C (concentration) is taken as 9 f/cc, and the value of Q is calculated based on the reported time since first exposure and the estimated average duration of exposure, using the equations presented in Section 5.1.2 of the main text. The results are shown in Figure A4-2. As seen, there is a clear increasing trend in mesothelioma incidence as a function of increasing cumulative exposure (C·Q).

Uncertainty and Bias Characterization

Appendix C discusses the primary sources of uncertainty in epidemiological studies of cancer risk from asbestos exposure in the workplace and describes the methods used in this document for characterizing the uncertainty. The following sections discuss the uncertainty characterization for the Ontario factory.

Uncertainty Due to Measurement Error

As described in Section 3.1 of Appendix C, all estimates of concentration levels of asbestos in the workplace are uncertain due to the combination of sampling error and analytical error. These measurements are usually averaged according to job or work area, often stratified by time. For this study, Finkelstein (1984) only provides mean concentrations for some years and operations. The magnitude of the uncertainty in the reported mean value for each job/time category (which is used to compute cumulative exposure) is a function of a) the number of samples used to compute the mean, b) the between-sample variability, and c) the nature of the underlying distribution. However, the authors do not provide information on the number of samples collected, or on the degree of between-sample variability. Therefore, in the absence of data, the default assumption described in Appendix C is applied to this study to account for measurement error, and is characterized as:

PDF(measurement error) ~ TRI(0.6, 1, 1.5)

Uncertainty in Mean Cumulative Exposure Values for Exposure Groups

The authors report CE values as bounded ranges for four exposure groups. As discussed in Appendix C, the uncertainty associated with use of the mid-point of the range as the mean exposure for the group is characterized as follows:

PDF(exposure, bounded) ~ TRI(Min/Mid, 1, Max/Mid)

The highest exposure group was characterized as unbounded range. As discussed in Appendix C, the point estimate and uncertainty is modeled as:

PDF(exposure, unbounded) ~ TRI(1, 5/3, 3)

Uncertainty in Conversion Factor from Dust Data (mppcf) to PCM f/cc

In this study, workplace air measurements were collected by stationary impingers for the years 1949, 1954, 1955, 1957, and semiannually during the 1960s. Starting in the last quarter of 1969, personal membrane sampling was implemented using personal monitors. No site-specific conversion factor for this facility is available. Therefore, as described in

Appendix C, a default factor of 3.0 was applied to this study, and the uncertainty around this value is characterized as follows:

PDF(conversion factor) ~ TRI(0.33, 1, 3.33)

Uncertainty in the Use of Stationary Rather Than Personal Air Monitors

Stationary air monitors were used at the Ontario plant until 1969. After this time, air measurements were collected with personal air monitors. For exposures prior to 1970, the use of stationary air monitors may tend to underestimate the true exposure level of workers, especially those engaged in activities that actively disturb asbestos-containing materials or dusts. As the cohort is defined as those workers employed prior to 1960, the air measurements collected during the period prior to 1969 is most representative of the workplace atmosphere. As described in Appendix C, uncertainty in cumulative exposure due to the use of stationary area monitors is characterized as:

PDF(personal vs. stationary) ~ BETA(2, 20, 0.9, 10)

Uncertainty in Temporal Representativeness

As noted above, the data used to estimate concentration values in the Ontario plant, which began operations in 1948, were collected at the plant for the period 1949 through 1979. The cohort evaluated by Finkelstein 1984 consisted of workers who first began employment prior to 1960, and follow-up was carried out through 1977 or 1980. Measurements prior to 1960 are sparse. Early exposures were based on assumptions weakly supported by these measurements. As discussed in Appendix C, when data are available at intermittent times over the exposure period, and the use of extrapolated data is moderate, the uncertainty is considered to be medium and is characterized as follows:

PDF(temporal representativeness) ~ TRI(0.8, 1, 1.2)

Bias Correction Factor for Data Reported as CE Rather Than CE10

This study reports cumulative exposure as CE rather than as CE10. As discussed in Appendix C, use of CE rather than CE10 tends to bias results low, with the magnitude depending on the duration of exposure, the length of follow-up, and whether or not early person years of observation were excluded. Finkelstein (1984) does not report the average duration, but based on the reported cumulative exposure of the cohort as 60 f/cc-yr and a calculated average from the concentrations reported by operation for the years

1949, 1969, and 1979, an average duration of 5.6 years was estimated. End of follow-up was either 1977 or 1981, as it occurred in two stages for this cohort, and the average time since last exposure was estimated to be 23 years. The mortality data by Finkelstein (1984) are standardized to the age and latency distribution of the total cohort for the period beyond 20 years from first exposure. Based on these study attributes a BCF for this cohort was determined to be:

$$BCF \sim TRI(1, 1, 1)$$

Effectively, for this study the bias associated with reporting cumulative exposure as CE rather than CE10 is negligible. The BCF ~ 1.0, and therefore it is not necessary to apply a BCF to this study.

Uncertainty in Cumulative Exposure for Mesothelioma Analysis

This study reports mesothelioma incidence as a mono-variate function of time since first exposure (T). The average value of cumulative exposure (C·Q) is estimated from the mid-point of the T bins (reported in Table 3 of Finkelstein 1984) and estimates of the average exposure concentration and average exposure duration for the entire cohort, as described above. As discussed in Section 3.7 of Appendix C, this approximation approach introduces uncertainty into the study-specific dose-response relationship, and this uncertainty may be approximated as follows:

$$PDF(\text{approximation of } C \cdot Q) \sim TRI\ (0.75, 1, 1.4)$$

Uncertainty in Fraction Amphibole

As discussed above, the fraction amphibole is estimated to be about 20% in one building at the factory and about zero in another building. Assuming that workers worked about equally in both buildings, the mean value of fraction amphibole is about 10% Clearly this estimate of the average fraction amphibole has wide uncertainty, since the assumption that all workers were exposed equally in both buildings is not based on any data. Therefore, the uncertainty bounds for the average fraction amphibole that the combined cohort was exposed to is assigned an estimated minimum of 5% and an estimated maximum of 15%:

$$PDF(f_{amph}) \sim TRI(0.05, 0.10, 0.15)$$

Uncertainty in Particle Size for Chrysotile

As mentioned above, the cement manufacturing plant evaluated by this study used only chrysotile asbestos in the board operation, and a mixture of chrysotile and crocidolite in the pipe production area. Of the TEM data sets available (see Appendix B), 11 are based on chrysotile asbestos. Three of these data sets correspond to the cement pipe manufacturing industry. These data sets differ by operation as mixing, forming, and finishing. Since Finkelstein (1984) does not categorize exposure groups by operation, there is no basis to select one TEM data set over the other. Therefore, the three chrysotile data sets based on cement pipe manufacturing were combined by averaging the fractions for each size bin of interest across operations. Since the assigned TEM data sets match on asbestos type and industry, the uncertainty in f_{size} for chrysotile is determined to be low for each cohort, and is modeled as follows:

$$PDF(f_{size[chrysotile]}) \sim TRI(0.8, 1, 1.2)$$

Uncertainty in Particle Size for Amphibole

Crocidolite asbestos was used in the pipe production process. Of the TEM data sets available (see Appendix B), 18 are based on amphibole asbestos. Three of these data sets are based on crocidolite asbestos, all for the industry of cement pipe manufacturing. These three data sets differ based on operation (mixing, forming, and finishing). As described above, there is no basis to assign a distribution based on a single operation to the cohort evaluated by Finkelstein (1984). As such, the three crocidolite TEM data sets based on cement pipe manufacturing where combined and applied to this study. As described in Appendix C, if TEM data sets are available that match on mineral form and industry, the uncertainty in f_{size} for amphibole is determined to be low, and is modeled as follows:

$$PDF(f_{size[amphibole]}) \sim TRI(0.8, 1.0, 1.2)$$

Figure A4-1. Lung Cancer Data for the Ontario Cement Plant

CE (PCM f/cc-yr)		Observed Deaths (a)	Expected Deaths (c)	Relative Risk		
Range (a)	Mean (b)			Pt. Est. (d)	5% LB	95% UB
0	0	3	2.3	1.3	0.5	3.1
0-30	15	3	1.3	2.3	0.8	5.4
30.1-75	52.55	6	1.0	6.2	3.0	11.5
75.1-105	90.05	5	0.4	12.1	5.5	23.8
105.1-150	127.55	5	0.6	9.0	4.1	17.7
>150	250	2	0.7	2.7	0.8	7.5

a) Data reported in Table 7 (Finkelstein 1984).

b) Calculated as the midpoint of the reported range of CE, except for the highest exposure group which has an unbounded range (5/3*lower bound).

c) Calculated value (observed deaths/relative risk).

d) Calculated value from mortality rates reported in Table 7 (Finkelstein 1984) (mortality rate for exposure group/mortality rate of Ontario males); Mortality rate for Ontario males reported as 1.3 per thousand man-years.

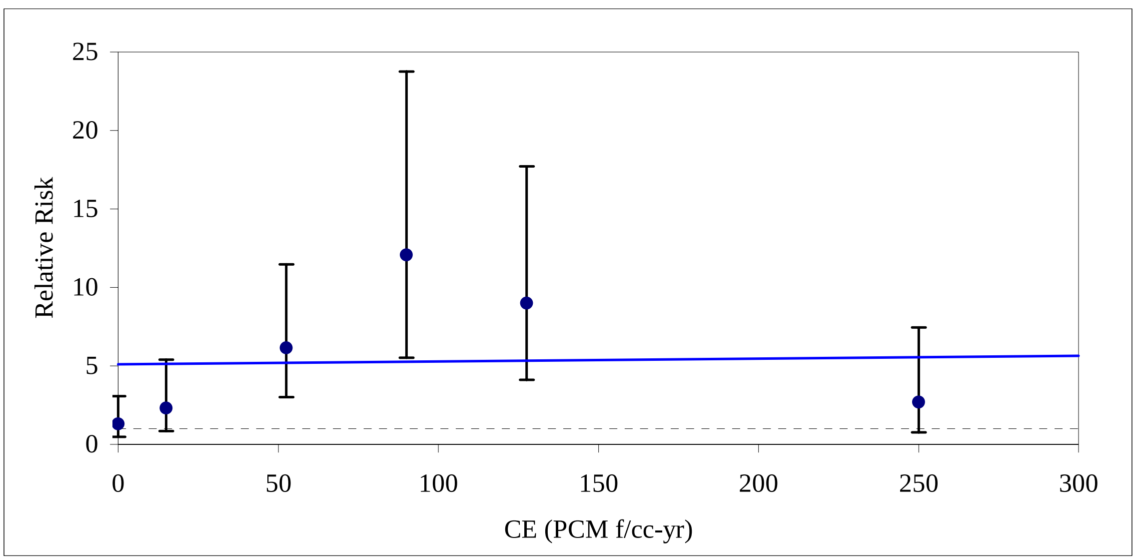
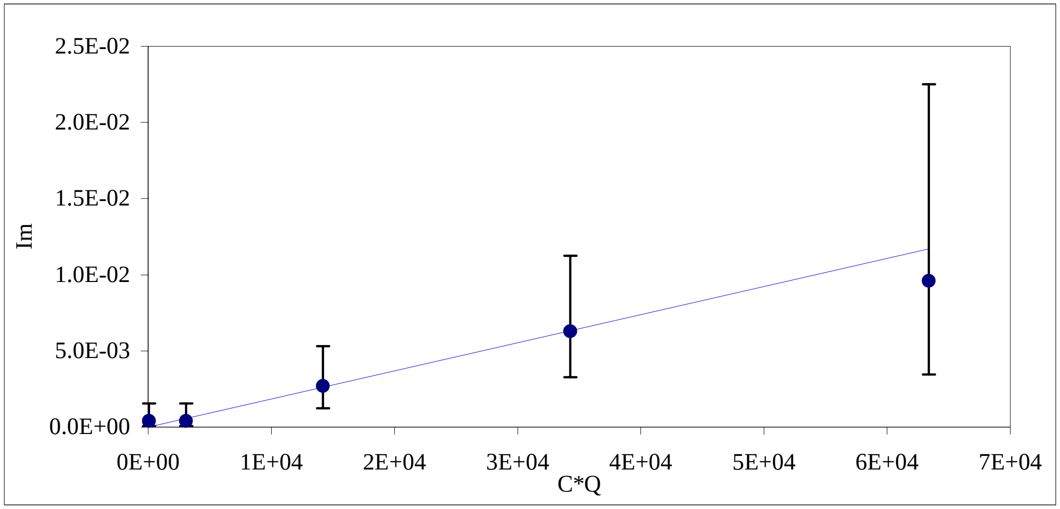


Figure A4-2. Mesothelioma Data for the Ontario Cement Plant

Yrs since first exposure		Average Cum. Exp. (f/cc-yr)(b)	Avg Conc (c)	Average Duration (d)	Q	Mortality Rate (a,e)	Observed Deaths (a,f)	PY (g)	Incidence (Im)	Uncertainty Bounds	
Range (a)	Mean									5% LB	95% UB
10-14	12	60	9	6.67	8	0.4	1	2500	4.0E-04	7.0E-05	1.6E-03
15-19	17	60	9	6.67	343	0.4	1	2500	4.0E-04	7.0E-05	1.6E-03
20-24	22	60	9	6.67	1576.3	2.7	5	1852	2.7E-03	1.2E-03	5.3E-03
25-29	27	60	9	6.67	3809.6	6.3	7	1111	6.3E-03	3.3E-03	1.1E-02
30-34	32	60	9	6.67	7043	9.6	3	313	9.6E-03	3.5E-03	2.3E-02

(a) Data reported in Finkelstein (1984) Table 3.
(b) Mean cumulative exposure for the cohort reported by Finkelstein 1984 (page 759).
(c) Average exposure for a subcohort of production workers reported by CHAP 1983
(d) Calculated as the average cumulative exposure divided by the average concentration (60 / 9).
(e) Mesothelioma deaths per 1000 person-years of observation.
(f) Observed mesothelioma deaths based on best evidence classification in production workers.
(g) Calculated as observed mesothelioma deaths divided by mesothelioma mortality rate.



A5. New Orleans Cement Products Manufacturing Plants

References

Primary: Hughes, J., Weill, H., and Hammad, Y. (1987). Mortality of workers employed in two asbestos cement manufacturing plants. *British Journal of Industrial Medicine* **44:**61-174.

Other: Hughes, J., and Weill, H. (1986). Asbestos exposure – quantitative assessment of risk. *American Review of Respiratory Disease* **133:**5-13.

Weill, H., Hughes, J., and Waggenspack, C. (1979). Influence of dose and fiber type on respiratory malignancy risk in asbestos cement manufacturing. *American Review of Respiratory Disease* **120:**345-354.

Hammad, Y.Y., Diem, J., and Weill, H. (1979). Evaluation of Dust Exposure in Asbestos Cement manufacturing Operations. *Am. Ind. Hyg. Assoc. J.* 40:490-495.

Study Description

Location and Facility Description

This facility includes two asbestos cement manufacturing plants located in New Orleans, Louisiana. Plant 1 is located in the commercialized area of the city, while plant 2 is located outside the city. The plants opened in the 1920s to manufacture cement building material. Plant 1 consists of one building, and produces flat shingles and corrugated sheets of cement asbestos board. Plant 2 consists of four separate buildings. Originally this plant only produced shingles, but production of other products (roofing materials, pipes, and asphalt flooring materials) were added, in that order, during the years of operation.

Asbestos Type

In plant 1, the primary asbestos type used in the cement products was chrysotile asbestos. However, amosite and crocidolite were also used in smaller amounts. The authors stated that amosite constituted about 1% of the mass of cement products manufactured in plant 1 from the early 1940s until the late 1960s. Crocidolite was used occasionally in the manufacturing of corrugated bulkhead for about ten years beginning in 1962, but no estimate of the amount of crocidolite used was provided. In plant 2, the pipe production department used both chrysotile and crocidolite, the latter of which constituted 3% of the final product. Only chrysotile asbestos was used in all other areas of plant 2.

Fraction Amphibole

The authors stated that the percentage of asbestos fiber in most asbestos cement products ranged from 15% to 28%. Using 21% as a representative value, point estimates for the fraction amphibole in these plants may be estimated as:

Plant 1 (amosite)	f_{amph} = 1% / 21% = 5%
Plant 2 (pipe production area)	f_{amph} = 3% / 21% = 14%
Plant 2 (other areas)	f_{amph} = 0%

However, as discussed in Appendix C, chrysotile is often contaminated with trace levels of tremolite amphibole. Based on the data summarized in Appendix C, the estimated average level of amphibole in plant 2 for workers in areas other than the pipe production area where only chrysotile asbestos was used is 0.054%.

Cohort Description and Follow-up

The study population was comprised of white and black men for whom a valid SSN could be obtained from company records and who were employed for at least one month during 1942-1969 (plant 1) or during 1937-1969 (plant 2). Women employees were excluded (N=321). In total, 7,098 workers qualified for the cohort. Workers who began work in plant 1 before 1942 (N=39) or in plant 2 before 1937 (N=128) were excluded, leaving 6,931 men, of whom 2,565 (37%) were employed in plant 1 and 4,366 (63%) in plant 2. Overall the population was 54% black and 46% white. Overall, approximately 60% of the cohort (including both plant 1 and plant 2 employees) worked for the cement manufacturing company for less than one year, and duration of employment on average was less than four years. Employees working in plant 2 (26.8 years) tended on average to begin work at an earlier age than plant 1 employees (31.7 years). The total number of person-years included in this cohort was not reported.

Follow-up was carried out up to 1982 or age 80, whichever came first. During this period, 2,143 total subjects were identified as dead, of which 2,014 (94%) death certificates were obtained.

Determination of Cause of Death and Diagnosis of Lung Cancer/Mesothelioma Cases

Death certificates were obtained from individual states and were coded by a nosologist according to the 8th Revision of the International Classification of Diseases (ICD). Certificates could not be obtained for 6% of the reported deaths. For these cases, deaths were allocated to categories of cause of death in the same proportion as those with certificates.

Reference Population

Hughes et al. (1987) evaluated the mortality experience of plant workers in comparison to both Louisiana rates, and national U.S. rates. Age adjusted Louisiana malignancy rates for the period 1960-1979 are higher than the national rates. Use of the U.S. rates rather than state rates resulted in lower expected numbers and therefore higher relative risks based on all cause deaths, deaths from malignancies, and specifically deaths from lung cancer. For the data included in the OSWER analysis, it is assumed that the authors are using Louisiana rates to calculate expected mortality, although this is not explicitly stated.

Estimating Exposure Concentration

From 1952 to 1969, measurements of airborne dust levels in each plant were made for each job by month and year using midget impingers (mppcf). Levels in the two plants were similar (Hughes et al. 1987). Anecdotal information from long-time workers was used to combine jobs in to categories of similar exposure levels and to compare relative conditions between the 1940s and 1950s. Estimated concentrations (mppcf) are summarized below:

Time Period	Mean Asbestos Concentration (mppcf)	
	Plant 1	Plant 2
1940-1949	10.0	8.0
1950-1959	7.2	9.1
1960-1969	1.3	3.9

Source: Hughes et al. (1987) (Table 2)

Beginning in 1969, measurements were performed using PCM-based membrane filter sampling. Conversion of previous dust levels (mppcf) into units of PCM f/cc was based on a site-specific conversion factor or 1.4 PCM f/cc per mppcf. This value was derived from 102 paired measurements made by midget impinger and PCM collected from various areas in one of these plants (Hammad et al. 1979).

Estimating Cumulative Exposure

Personnel records were used to compile dates of employment and a complete work history for each person. Copies of plant 2 Social Security Administration quarterly reports were also obtained to assess the completeness of employee identification for the years 1942, 1945, and 1948. Forms could not be obtained for plant 1 employees. The authors report a mean duration of employment of four years for both plants. All jobs in a category were assigned the same estimated concentration level, the mean of the available exposure measurements for that category. Details on specific job categories were not provided. Since plant 1 is comprised of one building where mixed asbestos types were used and there was only limited variability in recorded job titles, no attempt was made to categorize workers according to types of asbestos fiber exposure. However, plant 2 employees were categorized into two groups: those assigned to one or more jobs in the pipe production building where they would have been exposed to both chrysotile and crocidolite, and those who were never assigned to work in that building. This second group was assumed to have been exposed primarily to chrysotile asbestos.

Cumulative exposure for each worker for each person-year of observation was estimated by summing the concentration levels to which the worker was previously exposed, excluding the 10 most recent years.

The authors noted that anecdotal information provided by workers in plant 2 suggested that measurements of airborne dust levels in plant 2 may have tended to underestimate true long term average exposure levels. The authors stated that if the anecdotal information were used to adjust the measured values, the slope of the exposure-response curves in plant 2 might be about 1/2 as steep. In plant 1, anecdotal information had little effect on estimated exposure levels.

Smoking Data

A cross-sectional survey of workers in these plants in 1969 found 52% current smokers, 25% ex-smokers and 23% never-smokers in plant 1, and 49% current smokers, 26% ex-smokers and 25% never-smokers in plant 2. Estimates for the U.S. for 1969 are 55% current smokers. On this basis, it is concluded that the smoking rate in workers in both plants are similar to the general population.

Lung Cancer Results

The authors provide quantitative data on the relative risk of respiratory cancer (ICD162-163; according to ICD-8 this includes cancer of the trachea, bronchus, and lung, and cancer of the pleura) as a function of cumulative exposure in a subset of workers who were employed for a minimum of 6 months and for whom the follow-up period was at least 20 years. Raw data for respiratory cancer in each of the three sub-cohorts evaluated at the New Orleans cement factories are presented in Figures A5-1, A5-2, and A5-3. For employees in plant 1 (mixed chrysotile, amosite and crocidolite exposure), the relative risk of respiratory cancer shows only a slight tendency to increase as a function of increasing cumulative exposure. However, a relatively clear upward trend is observed for both of the plant 2 sub-groups (chrysotile exposure only, and chrysotile plus crocidolite exposures).

Hughes et al. (1987) report that plant 1 workers were similar to plant 2 workers with respect to employment duration, estimated exposure concentration, and years of hire. The authors discuss possible reasons for the differences in lung cancer risk between the two plants with respect to differences in the populations including average age at hire, size and racial composition of the workforce, physical layout of the plants, location of the plants, and smoking habits. The authors suggest that the majority of these factors were similar between plant populations and could not explain the differences seen in lung cancer risk. However, Hughes et al. (1987) do suggest that the differences in lung cancer risk between plants 1 and 2 may be due, at least in part, to the differing fiber types (as described above) used between the two plants. The authors note that more amphibole was used in the plant 2 pipe area than in plant 1, and that this use of crocidolite in plant 2 may explain the increased risk of lung cancer seen in plant 2 employees. However, similar risk was demonstrated between the two sub-cohorts in plant 2 exposed either only to chrysotile, or to chrysotile and crocidolite. In this regard the authors suggest a confounding effect associated with unknown differences including personal factors or undetected differences in working conditions between those working in the pipe area and those not.

Mesothelioma Results

As mentioned previously, the primary cohort evaluated in this study was comprised of workers initially employed during 1942-1969 in plant 1, or during 1937-1969 in plant 2. Within this group, six pleural mesothelioma cases occurred by the end of 1981, two among plant 1 workers, the other four among plant 2 workers. In addition, four other mesothelioma cases occurred in plant 2 workers that were not considered members of the primary cohort. Three of these cases (two pleural, one peritoneal) were observed to occur after the end of the follow-up period, whereas the other one case (pleural) occurred in a man initially employed before 1937. Of the 10 total mesothelioma cases, the two plant 1 employees were employed only for short periods (<10 months), and one of them may have been previously exposed to asbestos as a longshoreman. Of the eight cases among the plant 2 employees, seven were employed in the pipe production area and thus were exposed to a mixture of both chrysotile and crocidolite. The remaining case had been employed for 43 years in the shingle production area, indicating exposure to only chrysotile asbestos. The authors interpreted the data to indicate that there is a higher risk of mesothelioma from exposure to amphibole asbestos than chrysotile asbestos, but recognized that differences in exposure duration might also be a factor. Therefore, a case-control study was conducted to evaluate the possibility that the higher risk to pipe production workers was a consequence of longer durations (on average the pipe area workers were employed four times longer than other workers) rather than exposure to crocidolite. A significant relationship between mesothelioma risk and both assignment to the pipe area and proportion of employment spent in this area was observed, consistent with the hypothesis that crocidolite asbestos used in pipe manufacture conveys a higher mesothelioma risk than chrysotile.

Although the authors reported time since first exposure and duration of exposure for each of the 10 mesothelioma cases described above, data for the cohort on time since first exposure, exposure level and on total person-years of observation were not reported. Therefore, the mesothelioma data from this study can not be included in the data set used for fitting.

Uncertainty and Bias Characterization

Appendix C discusses the primary sources of uncertainty in epidemiological studies of cancer risk from asbestos exposure in the workplace and describes the methods used in this document for characterizing the uncertainty. The following sections discuss the uncertainty characterization for this study.

Uncertainty Due to Measurement Error

As described in Section 3.1 of Appendix C, all estimates of concentration levels of asbestos in the workplace are uncertain due to the combination of sampling error and analytical error. These measurements are usually averaged according to job or work area, often stratified by time. For this study, Hughes et al. (1987) report mean concentrations as a function of time period for each plant (see Table 3 in the original report). The magnitude of the uncertainty in the reported mean value for each job/time category (which is used to compute cumulative exposure) is a function of a) the number of samples used to compute the mean, b) the between-sample variability, and c) the nature of the underlying distribution. The authors report 100 measurements were collected in plant 1 and 1,664 measurements were collected in plant 2. However, the authors do not provide information on the degree of between-sample variability. Therefore, in the absence of data, the default assumption described in Appendix C is applied to this study to account for measurement error, and is characterized as:

PDF(measurement error) ~ TRI(0.6, 1, 1.5)

Uncertainty in Mean Cumulative Exposure Values for Exposure Groups

At Plant 1, the authors report the mean CE10 value for all exposure groups, so no uncertainty distribution is needed to account for uncertainty due to use of the mid-point of each range to estimate the true mean. For Plant 2, CE10 values are reported as ranges. For groups with bounded ranges, the mid-point of the range is taken as the point estimate. As discussed in Appendix C, this point estimate is an uncertain estimate of the true mean, and the uncertainty is characterized as follows:

PDF(exposure, bounded) ~ TRI(Min/Mid, 1, Max/Mid)

The highest exposure groups for both of the Plant 2 cohorts have an unbounded upper range. As described in Appendix C, the point estimate and uncertainty for these groups is modeled as:

PDF(exposure, unbounded) ~ TRI(1, 5/3, 3)

Uncertainty in Conversion Factor (CF) from Dust Data (mppcf) to PCM f/cc

In this study, conversion of previous dust levels (mppcf) into units of PCM f/cc was based on a site-specific conversion factor or 1.4 PCM f/cc per mppcf. This value was derived from 102 paired measurements made by midget impinger and PCM collected from five areas in Plant 1 (Hammad et al. 1979). The data are summarized below:

Area	Number of Paired Samples	Impinger (mppcf)		PCM (f/cc)		Mean Ratio	Correl. Coeff.
		Mean	Stdev	Mean	Stdev		
1	23	0.50	0.34	0.23	0.068	0.63	0.18
2	27	0.91	0.92	1.2	1.9	1.3	0.91
3	14	0.40	0.18	0.38	0.11	1.1	0.31
4	23	1.3	1.5	3.5	5.5	2.5	0.47
5	15	0.64	0.62	0.46	0.21	1.5	0.31
All	102	0.79	0.94	1.3	3.0	1.4	0.57

Although the authors report the mean ratio (1.4 PCM f/cc per mppcf), the standard deviation (uncertainty) of the ratio is not reported. However, because the correlation coefficients between paired dust and filter samples were reported, the uncertainty around the mean ratio can be reconstructed using Monte Carlo simulation. This is done by assuming each distribution is lognormal, drawing many correlated data pairs for each location, calculating the ratio for each paired draw for each location, and then averaging the ratios across locations. Based on this approach, uncertainty in the average CF at this site may be expressed as:

PDF ~ LN(1.57, 0.81)

Because the mean CF selected by the authors was 1.4, uncertainty in the point estimate of cumulative exposure due to uncertainty in the CF may be expressed as:

PDF(conversion factor - plant 1) ~ LN(1.57, 0.81) / 1.4 = LN(1.12, 0.58)

The CF selected by the authors of 1.4 is based only on measurements collected in plant 1. Therefore, the above uncertainty distribution is applied only to the plant 1 sub-cohort. As reported in Hughes et al. (1987) average estimated exposure concentration was similar between the two plants. Therefore, rather than apply the default conversion factor of 3.0 in the absence of a study-specific conversion factor (as described in Appendix C), this same conversion factor is applied to the sub-cohorts in plant 2. The uncertainty around the CF for the plant 2 sub-cohorts is specified with a wider uncertainty bound, and is characterized as:

PDF(conversion factor - plant 2) ~ LN(1.12, 1.0)

Uncertainty in the Use of Stationary Rather Than Personal Air Monitors

In this study, measures of asbestos in air were based on stationary monitors placed at various locations around the factory. As discussed in Appendix C, use of stationary monitors may tend to underestimate the true exposure level of workers, especially those engaged in activities that actively disturb asbestos-containing materials or dusts. Based on available data on the ratio of particulate concentrations measured using personal to stationary monitors at various locations, the uncertainty attributable to this source may be characterized as:

PDF(personal vs. stationary) ~ BETA(2, 20, 0.9, 10)

Uncertainty in Temporal Representativeness

For this study, dust and/or PCM measurements are available from 1952 forward. However, the cohorts being evaluated were exposed from either 1937-1969 (plant 1) or from 1942-1969 (plant 2). Thus, data on concentration levels are extrapolated for about 1/3 of the study period, and are measured for about 2/3 of the study period. Based on this, uncertainty in temporal representativeness is ranked as moderate, and is characterized by:

PDF(temporal representativeness- plant 1) ~ TRI(0.8, 1, 1.2)

This distribution is applied to workers in Plant 1. In Plant 2, anecdotal information suggested that true dust levels might be about twice as high as measured air levels used to compute CE10 values. To account for this, an additional uncertainty distribution is used, as follows:

PDF(temporal representativeness - plant 2) ~ TRI(0.8, 1, 1.2) · U(1, 2)

Bias Correction Factor in Data Reported as CE Rather Than CE10

Hughes et al. (1987) report lung cancer mortality by cumulative exposure lagged by ten years, so no BCF is required for this cohort.

Uncertainty in Fraction Amphibole

Three cohorts were evaluated in this study, stratified based on the level and type of amphibole used in the workplace:

- Cohort 1 = Workers in plant 1 exposed primarily to chrysotile, with low levels of amosite (estimated to average about 5% of the asbestos mixture, plus an additional contribution from crocidolite (amount not specified)). Because the information on f_{amph} is based on descriptions of relative mass rather than any direct particles counts in workplace air, uncertainty is ranked as medium, and is characterized as:

  PDF(f_{amph}) ~ TRI (0.03, 0.05, 0.07)

- Cohort 2 = Workers in plant 2 exposed only to chrysotile. As discussed in Appendix C, available data suggest that "pure" chrysotile may contain trace levels of amphibole contamination, so uncertainty around f_{amph} for this cohort is modeled as:

  PDF(f_{amph}) ~ LOGNORMAL(0.00054, 0.001)

- Cohort 3 = Workers in the pipe section of plant 2 exposed to chrysotile plus about 14% crocidolite. Because the information on f_{amph} is based on descriptions of relative mass rather than any direct particles counts in workplace air, uncertainty is ranked as medium, and is characterized as:

$$PDF(f_{amph}) \sim TRI(0.11, 0.14, 0.20)$$

Uncertainty in Particle Size for Chrysotile

For this study, the primary type of asbestos used at the cement manufacturing plants was chrysotile. Of the TEM data sets available (see Appendix B), 11 are based on chrysotile asbestos. Three of these data sets correspond to the cement manufacturing industry. These data sets differ by operation as mixing, forming, and finishing. As Hughes et al. (1987) do not specifically detail the operations conducted at the New Orleans Plants, there is no basis for selecting any one of the three cement industry data sets over the other. Therefore, the three cement industry data sets were combined. Since the assigned TEM data sets match on asbestos type and industry, the uncertainty in f_{size} for chrysotile is determined to be low for each cohort and is characterized by:

$$PDF(f_{size[chrysotile]}) \sim TRI(0.8, 1, 1.2)$$

Uncertainty in Particle Size for Amphibole

Of the TEM data sets available (see Appendix B), 18 are based on amphibole asbestos. As described in Appendix C, decisions for assigning matched TEM distributions to each of the three cohorts presented in this study are based on the closest match to the cement manufacturing industry and then on the closest match to the amphibole form. For each of the three cohorts, the bases for these assignments are described below.

<u>Cohort 1 (Plant 1 workers)</u>. Workers in Cohort 1 were exposed to both amosite and crocidolite. Of these two forms, amosite was used in larger amounts and for a longer time than crocidolite. Of the 18 TEM data sets for amphibole asbestos, five are based on amosite, but none of these are from cement industry locations. These data sets are based on mining/milling and insulation manufacturing. There are 3 data sets for crocidolite from cement industry locations. The data sets differ by operation (preparation, finishing, and dumping). Mortality data are not categorized by operation, so these three data sets were combined with the five amosite data sets to

represent the particle size distribution for amphibole exposures for Cohort 1. In accord with the table above, uncertainty is rated as medium and is represented by:

$$PDF(f_{size[amphibole]}) \sim TRI(0.5, 1, 1.5)$$

Cohort 2 (Plant 2 chrysotile only). According to Hughes et al. (1987), Plant 2 workers who were never employed in the pipe production area (cohort 2) were exposed to only chrysotile asbestos. However, as described in Appendix C and detailed in Addison and Davies (1990), tremolite may occur as a contaminant in chrysotile asbestos. There is only one TEM data set for tremolite asbestos, but this is based on the mining/milling industry and not the cement manufacturing industry. In accord with the general approach described in Appendix C, when the TEM data set matches on amphibole type but not industry, uncertainty is ranked as medium and is characterized by:

$$PDF(f_{size[amphibole]}) \sim TRI(0.5, 1, 1.5)$$

Cohort 3 (Plant 2 pipe area workers). Workers in Plant 2 who were employed in the pipe production area (cohort 3) were exposed to crocidolite asbestos. The three available data sets for crocidolite asbestos in plants manufacturing asbestos-cement products were combined by averaging the size bins across operations to represent the particle size distribution for amphibole exposures for Cohort 3. In accord with the approach described in Appendix C, uncertainty is rated as low and is represented by:

$$PDF(f_{size[amphibole]}) \sim TRI(0.8, 1, 1.2)$$

Figure A5-1. Lung Cancer Data for Workers Employed in Plant 1 of the New Orleans Cement Products Manufacturing Plant.

CE10 (mppcf-yr)		CE10 (PCM f/cc-yr)	Observed	Expected	Relative Risk		
Range (a)	Mean (a)	Mean (b)	Deaths (a)	Deaths (a)	Point Est	5% LB	95% UB
< 6	4	5.6	3	2.9	1.0	0.4	2.4
6-24	13	18.2	9	8.0	1.1	0.6	1.9
25-49	35	49	2	3.7	0.6	0.2	1.5
50-99	74	103.6	3	3.8	0.8	0.3	1.9
>=100	183	256.2	5	4.1	1.2	0.6	2.4

a) Data reported in Table 8 (Hughes et al. 1987).

b) A conversion factor of 1.4 based on dust and filter measurements (Hammad et al. 1979) was used to convert CE10 values to units PCM f/cc-yr.

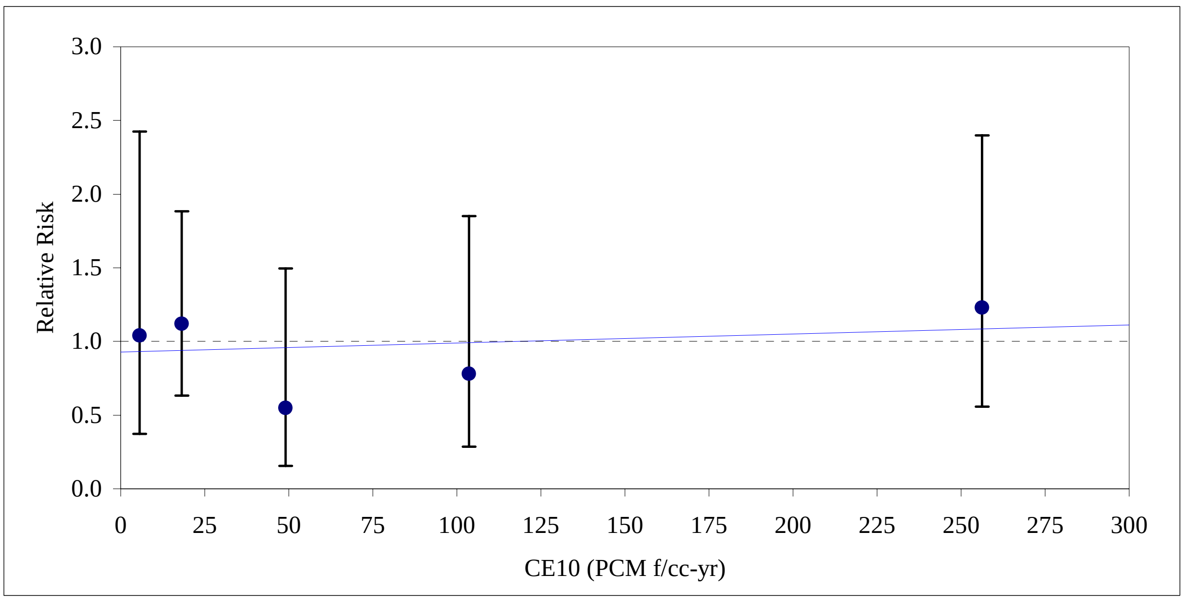


Figure A5-2. Lung Cancer Data for Workers Employed in Plant 2 of the New Orleans Cement Products Manufacturing Plant Exposed Only to Chrysotile Asbestos.

CE_{10} (mppcf-yr)		CE_{10} (PCM f/cc-yr)	Observed	Expected	Relative Risk		
Range (a)	Mean (b)	Mean (c)	Deaths (a)	Deaths (a)	Point Est.	5% LB	95% UB
<3	2	2.1	8	8.8	0.9	0.5	1.6
3-5	4	5.6	8	7.0	1.1	0.6	2.0
6-24	15	21	17	11.1	1.5	1.0	2.2
25-49	37	51.8	5	2.9	1.7	0.8	3.4
>=50	83.3	116.7	4	2.6	1.6	0.6	3.3

a) Data reported in Table 11 (Hughes et al. 1987).

b) Calculated as the midpoint of the reported range of CE10, except for the highest exposure group which assigns a point estimate value = 5/3*lower bound.

c) A conversion factor of 1.4 based on dust and filter measurements (Hammad et al. 1979) was used to convert CE10 values to units PCM f/cc-yr.

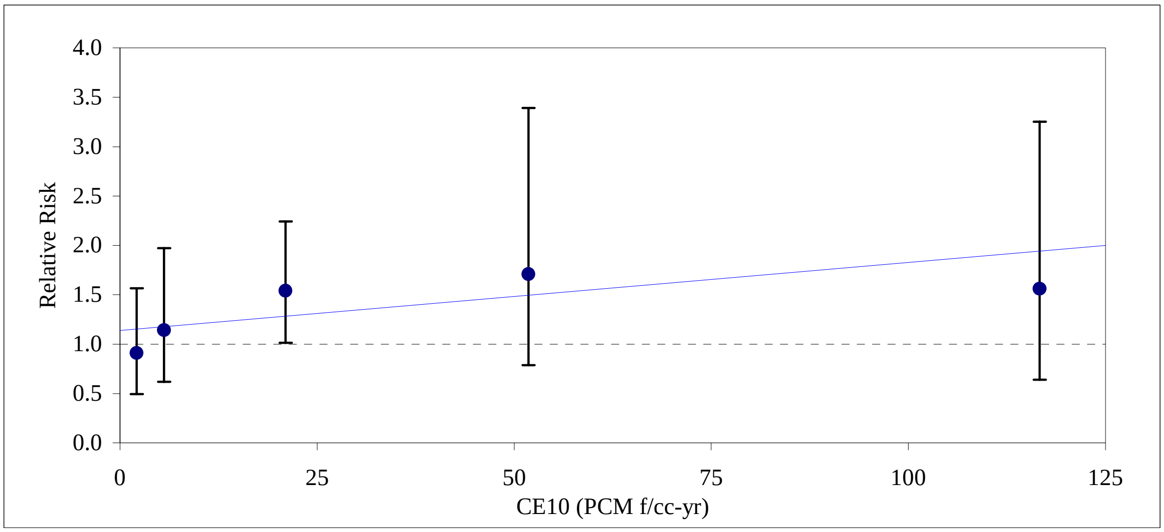


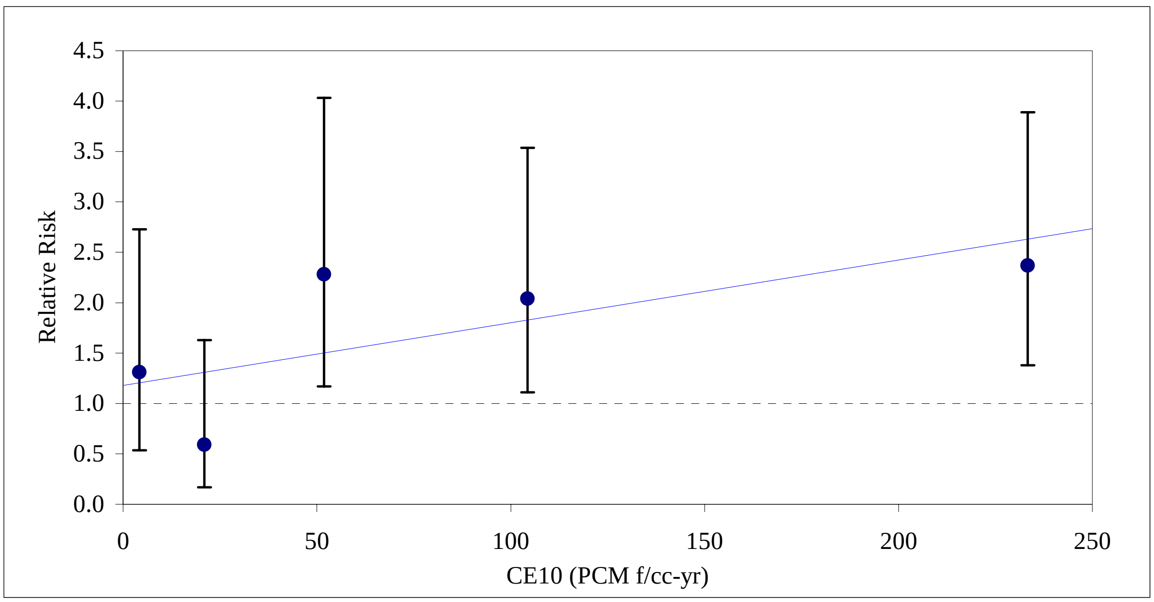
Figure A5-3. Lung Cancer Data for Workers Employed in Plant 2 of the New Orleans Cement Products Manufacturing Plant Exposed to Chrysotile and Crocidolite Asbestos.

CE_{10} (mppcf-yr)		CE_{10} (PCM f/cc-yr)	Observed	Expected	Relative Risk		
Range (a)	Mean (b)	Mean (c)	Deaths (a)	Deaths (a)	Point Est.	5% LB	95% UB
< 6	3	4.2	4	3.1	1.3	0.5	2.7
6-24	15	21	2	3.4	0.6	0.2	1.6
25-49	37	51.8	7	3.1	2.3	1.2	4.0
50-99	75	104.3	8	3.9	2.0	1.1	3.5
>=100	166.7	233.3	10	4.2	2.4	1.4	3.9

a) Data reported in Table 11 (Hughes et al. 1987).

b) Calculated as the midpoint of the reported range of CE10, except for the highest exposure group which assigns a point estimate value = 5/3*lower bound.

c) A conversion factor of 1.4 based on dust and filter measurements (Hammad et al. 1979) was used to convert CE10 values to units PCM f/cc-yr.



A6. Quebec Mines and Mills

References

Primary: McDonald, J., Liddell, F., Dufresne, A, and McDonald, A. (1993). The 1891-1920 birth cohort of Quebec chrysotile miners and millers: mortality 1976-1988. *British Journal of Industrial Medicine*, **50**: 1073-1081.

Other: Liddell, F., McDonald, A., and McDonald, J. (1997). The 1891-1920 birth cohort of Quebec chrysotile miners and millers: development from 1904 and mortality to 1992. *Annals of Occupational Hygiene*, **41**(1): 13-36.

Begin, R., Gauthier, J.J., Desmeules, M., and Ostiguy, G. (1992) Work-related mesothelioma in Quebec, 1967-1990. *American Journal of Industrial Medicine* **22**:531-542.

Case, B. and Sebastien, P. (1987). Environmental and occupational exposures to chrysotile asbestos: A comparitive microanalytic study. *Archives of Environmental Health,* **42**: 185-191.

Case, B.W. and Sebastien, P. (1989). Fibre levels in lung and correlation with air samples. In: Bignon, J., Saracci, R., eds. *Non-Occupational Exposure to Mineral Fibres.* Vol. 90: 207-218

Dagbert, M. (1976). Etude de correlation des mesures d'empoussierage dans l'industrie de l'amiante. Document 5. Quebec Comite d'etude sur la salubrite dans l'industrie de l'amiante (President: rene Beaudry, jcp).

Gibbs, G.W. and Lachance, M. (1972) Dust exposure in the chrysotile asbestos mines and mills of Quebec. *Archives of Environmental Health*, **24**: 189-197.

Gibbs, GW (1994), The assessment of exposure in terms of fibres. *Ann Occup. Hygiene,* **38:** 477-487**.**

Liddell, F., McDonald, J., and Thomas, D. (1977). Methods of cohort analysis: appraisal by application to asbestos mining. *J. R. Statistical Society A*, **140**: 469-491.

Liddell, F., Thomas, D.C., Gibbs, G.W., and McDonald, J.C. (1984). Fibre exposure and mortality from pneumoconiosis, respiratory and abdominal malignancies in chrysotile production in Quebec, 1926-1975.

McDonald, J., Liddel, F., Gibbs, G., Eyssen, G., and McDonald, A. (1980). Dust exposure and mortality in chrysotile mining, 1910 – 1975. *British Journal of Industrial Medicine*, **37**: 11-24.

McDonald, J., McDonald, A., Gibbs, G., Siematycki, J., and Rossiter, C. (1971). Mortality in the chrysotile asbestos mines and mills of Quebec. *Archives of Environmental Health*, **22**: 677-686.

McDonald, J., Rossiter, C., Eyssen, G., and McDonald, A. (1973). Mortality in the chrysotile producing industry of Quebec: a progress report. In: *Proceedings of the IVth International Pneumoconiosis Conference, Bucharest, 1971*, pp. 232- 237. Apimondia, Bucharest.

Stayner, L.T., Dankovic, D.A., and Lemen, R.A. (1996). Occupational exposure to chrysotile asbestos and cancer risk: a review of the amphibole hypothesis. American Journal of Public Health, 86(2): 179-186.

Williams-Jones AE, Normand C; Clark JR; Vali H; and Martin RF. 2001. Controls of Amphibole Formation in Chrysotile Deposits: Evidence from the Jeffrey Mine, Asbestos, Quebec. *The Canadian Mineralologist*, Special Publication 5, pp. 89-104.

Study Description

Location and Facility Description

There are a number of asbestos mines and mills located in Quebec, Canada. One location included a number of small mines located near the community of Thetford, about 90 km south of the city of Quebec. A second location was a mine 60 km southwest of Thetford in a town named Asbestos, near the community of Danville. Production at the mines began before 1900. By 1918, the region was producing around 165,000 tons of fiber a year. These mining operations in Quebec produced most of the world's supply of asbestos until after World War II. Production continued to expand into the 1980s to approximately 1.3 million tons per year (Liddell et al. 1997). In addition to the mines, a small factory manufacturing asbestos products was opened by the company operating the Asbestos mine.

Asbestos Type

The primary type of asbestos collected from the Quebec mines is chrysotile.

Fraction Amphibole

As noted above, the mines and mills in Quebec produce chrysotile asbestos. However, most chrysotile deposits also contain low levels of amphibole (tremolite) (e.g., Addison and Davies 1990), including the deposits in Quebec (Williams-Jones et al. 2001). Case and Sebastien (1989) collected samples of ambient air at Thetford and Asbestos and analyzed these by TEM. The results are summarized below:

		Concentration (f/L)				
		Raw data		Minus Bkg		
Location	Type	Chrysotile	Tremolite	Chrysotile	Tremolite	f(amph)
Control	Ambient	0.7	nd	0		
Asbestos	Ambient	33	0.2	32.3	0.2	0.6%
Thetford	Ambient	40	1.5	39.3	1.5	3.7%

Based on these data, the point estimate for fraction amphibole is 0.6% in Asbestos and 3.7% in Thetford.

Cohort Description and Follow-up

Observations on mortality among Quebec miners and millers have been published on several occasions. The first was based on 2,413 deaths to November 1966 (McDonald et al., 1971). Others included 3,216 deaths to 1970 (McDonald et al., 1973), then 4,037 deaths to 1974 (Liddell et al., 1977), and then on 4,463 deaths to 1976 (McDonald et al., 1980). All of these previous reports were based on a birth cohort consisting of approximately 11,000 men (and some 440 women) who were born between 1891 and the end of 1920 that had been employed for at least 1 month. The initial size of the cohort has reduced over time based on findings that some men had more than one work record. No trace was ever found on 1,026 men, and a further 64 had been lost to follow-up.

The evaluation by McDonald et al. (1993) was based on 5,351 men known to be alive by the end of 1976 (the previous follow-up period). These men are included in the defined birth cohort as described above, which included 10,925 persons based on a best estimate by McDonald et al. (1993). Of these surviving men, all but 16 men were traced. Follow-up included 2,758 from mines and mills in the region of Thetford Mines, 2,158 from the mine and mill in Asbestos, and 419 from the small asbestos products factory. These data are included in the current fitting effort. Further follow-up was carried out by Liddell et al. (1997) on an initial birth cohort of 10,918 men to May 31, 1992. Of these men, Liddell et al. (1997) reported 82% mortality (8009 deaths). These follow-up data were not included in the current fitting effort because mortality was presented for the entire cohort and was not stratified according to location (i.e., Thetford Mines, Asbestos Mines, and Asbestos Factory).

Determination of Cause of Death and Diagnosis of Lung Cancer/Mesothelioma Cases

Cause of death was obtained from death certificates where available. Death certificates were found for 98.4% of the 5,351 surviving men evaluated by McDonald et al. (1993). Certificates were coded according to the 8th or 9th Revisions of the International Classification of Diseases (ICD). Some information on cause of death was obtained for 33 of the remaining 46 deaths. The authors used the available information to code these deaths. Diagnoses of mesothelioma deaths were supported by careful scrutiny of all related clinical, biopsy, and necropsy records.

Reference Population

Expected mortality was based on Quebec death rates. Rates for the six year period from 1980 to 1985 were the most recent available to McDonald et al. (1993). Therefore, rates from this period were used to give estimates for 1986, 1987, and 1988.

Estimating Exposure Concentration

Estimates of dust levels in specific jobs were based on data from over 4,500 midget impinger measurements collected systematically from 1949 to 1966. McDonald et al.

(1993) does not mention the procedure for extrapolation for the period prior to 1948. However, Liddell et al. (1984) stated that for this period, estimates were based on interviews with long-term employees and comparison with more recent conditions. McDonald et al. (1993) estimated the trends in dust concentration year by year from 1967 onward based on available information as provided in Gibbs and Lachance (1972).

Conversions between dust levels and PCM concentrations were derived from 623 paired side-by-side samples. Gibbs evaluated these data and concluded " there is no single overall conversion factor that can be applied to the mine and mill data." Gibbs discusses the Liddell et al. (1984) job-specific conversion factors that were in the order of magnitude of 3.67, 3.57, 3.46 and 3.44 PCM fibers/mL. He compared them to his samples and conducted an analysis showing that the upper bound of the 95% confidence interval for an overall conversion factor would be approximately 3.64. This factor was applied to this study to convert from reported measure of exposure expressed as mppcf-yrs to f/cc-yrs.

Estimating Cumulative Exposure

Cumulative exposures were estimated based on detailed work histories for each man in the cohort. These histories were first recorded in 1904, and were updated to 1985 from medical records or employment records. Each man's dust exposure was calculated accumulated to age 55, because by this age McDonald et al. (1993) postulate that most men would have received a high proportion of their lifetime exposure. All men were over 55 years of age by the end of 1976. For each employee, McDonald et al. (1993) accounted for the fraction of the year worked, the average dust concentration for the particular job and year, and the weekly hours worked during the period in question. However, unrecorded movement of personnel between the mine and mill and the factory in Asbestos, Quebec was reported by Liddell et al. (1997) to occur frequently. This effect makes the exposure estimates more uncertain and may lead to exposure misclassification, but without quantitative data, the extent to which this unaccounted movement may impact the exposure estimates is unknown.

Smoking Data

Information on smoking habits was obtained from questionnaires in 1970. For those men who died since 1950, the questionnaire was completed by proxies. McDonald et al.

(1993) reported smoking data for all of the deaths except 273 men for whom information was insufficient to allocate them to any of the classes. One thousand and ten men were classified as non-smokers, 1,138 as ex-smokers, 1,119 men as smoking <20 cigarettes a day, and 1,795 men as smoking more than 20 cigarettes a day.

By smoking alone, there was a dose- response for all causes and for lung cancer. Cross-analyzing by smoking and asbestos exposure for lung cancer showed a small effect for asbestos exposure and a larger effect for smoking. The smoking effect on lung cancer seemed about 5 times greater than asbestos exposure.

Lung Cancer Results

Data for lung cancer (ICD 162; ICD-8 and ICD-9 categorize as cancer of the trachea, bronchus, and lung) extrapolated from Table 5 of McDonald et al. (1993) are presented in Figure A6-1 for workers at the Asbestos mines site, in Figure A6-2 for workers at the Thetford mine site, and in Figure A6-3 for workers at the asbestos factory in Asbestos. As seen, there was no clear exposure-response trend in the Asbestos mine, but there was an upward trend in the Thetford mine and the factory in Asbestos.

Mesothelioma Results

McDonald et al. (1993) reported six mesothelioma deaths in the Asbestos mine and mill, 14 mesothelioma deaths in the Thetford Mines, and five in the asbestos factory. However, no data on mesothelioma incidence as a function of time since first exposure or duration of exposure were reported, so these results were not included when fitting the quantitative mesothelioma exposure-response model.

Uncertainty and Bias Characterization

Appendix C discusses the primary sources of uncertainty in epidemiological studies of cancer risk from asbestos exposure in the workplace and describes the methods used in this document for characterizing the uncertainty. The following sections discuss the uncertainty characterization and issues of potential bias for this study.

Uncertainty Due to Measurement Error

As described in Section 3.1 of Appendix C, all estimates of concentration levels of asbestos in the workplace are uncertain due to the combination of sampling error and analytical error. These measurements are usually averaged according to job or work area, often stratified by time. The magnitude of the uncertainty in the reported mean value for each job/time category (which is used to compute cumulative exposure) is a function of a) the number of samples used to compute the mean, b) the between-sample variability, and c) the nature of the underlying distribution. However, McDonald et al. (1993) do not report concentration data and do not provide information on the number of samples collected, or on the degree of between-sample variability. Therefore, in the absence of data, the default assumption described in Appendix C is applied to this study to account for measurement error, and is characterized as:

PDF(measurement error) ~ TRI(0.6, 1, 1.5)

Uncertainty in Mean Values for Exposure Groups

The authors report CE values as ranges for the four exposure groups for each mining location. For the three exposure groups with bounded ranges, the mid-point of the range is taken as the point estimate. As discussed in Appendix C, this point estimate is an uncertain estimate of the true mean, and the uncertainty is characterized as follows:

PDF(exposure, bounded) ~ TRI(Min/Mid, 1, Max/Mid)

For the highest exposure group, the range was unbounded (≥ 300 f/cc-yr). As discussed in Appendix C, in this case the point estimate and uncertainty are modeled as:

PDF(exposure, unbounded) ~ TRI(1, 5/3, 3)

Uncertainty in Conversion Factor (CF) from Dust Data (mppcf) to PCM f/cc

A substantial data set of midget impinger and membrane filter samples collected at mining locations in Quebec have been reported and evaluated by Gibbs and LaChance (1974), Dagbert (1976), McDonald et al. (1980), and Gibbs (1994). The CF varies substantially from mine to mine and from operation to operation, and correlation coefficients between dust and fiber measurements are generally low. After log-transformation, the average relationship is approximately linear, which yields an exponential relationship in linear space:

$y = a \cdot x^b$

where

y = concentration expressed at PCM f/cc
x = concentration expressed as mppcf

The uncertainty bounds around the conversion factor (y/x) at any particular concentration value are quite wide, approximately 100-fold (Gibbs 1994, Doll and Peto 1985), with the following parameters:

b = 0.68
a(best estimate) = 10.97
a(lower bound) = 0.58
a(upper bound) = 55.7

Based on this model, the ratio of the upper bound and the lower bound to the best estimate of the conversion factor for any value of x is given by:

CF(ub) / CF(be) = a(upper bound) / a(best estimate) = 5.08
CF(lb) / CF(be) = a(lower bound) / a(best estimate) = 0.053

Thus, uncertainty in the CF at this site may be expressed as:

PDF(conversion factor) ~ TRI(0.053, 1, 5.08)

Uncertainty in the Use of Stationary Rather Than Personal Air Monitors

McDonald et al. (1993) do not report the use of personal air monitors at this mining facility. In the absence of knowledge, it is assumed the measures were collected using stationary monitors. As discussed in Appendix C, use of stationary monitors may tend to underestimate the true exposure level of workers, especially those engaged in activities that actively disturb asbestos-containing materials or dusts. Based on available data on the ratio of particulate concentrations measured using personal to stationary monitors at various locations, the uncertainty attributable to this source may be characterized as:

PDF(personal vs. stationary) ~ BETA(2, 20, 0.9, 10)

Uncertainty in Temporal Representativeness

As mentioned previously, the data used to estimate concentration values at the Quebec mines were primarily collected at the factory for the period between 1949 and 1966. For the period prior to 1949, concentration estimates were made based on interviews with long-term employees and information of more recent conditions. As discussed in Appendix C, when data are moderately representative of the exposure period of employees, and data must be extrapolated from other sources to account for data gaps, the uncertainty associated with the temporal representativeness is considered to be medium, and is characterized as follows:

PDF(temporal representativeness) ~ TRI(0.8, 1, 1.2)

Bias Correction Factor for Data Reported as CE Rather Than CE10

This study reports cumulative exposure as CE rather than as CE10. As discussed in Appendix C, use of CE rather than CE10 tends to bias results low, with the magnitude depending on the duration of exposure, the length of follow-up, and whether or not early person years of observation were excluded. McDonald et al. (1993) does not report the average duration, and data are not presented in a form for calculating an average duration. Therefore, an average duration of 7 years was applied to this study as an estimated value with large uncertainty associated. The mortality data by McDonald et al. (1993) are reported for 20 years or more after first employment. Based on these study attributes, a BCF for this cohort was estimated as described in Appendix C to be:

BCF ~ TRI(1, 1, 1)

Effectively, for this study the bias associated with reporting cumulative exposure as CE rather than CE10 is negligible. The BCF ~ 1.0, and therefore it is not necessary to apply any BCF to this study.

Uncertainty in Fraction Amphibole

As noted above, the Quebec mines are chrysotile mines. Studies have found tremolite contamination in the ambient air around the Quebec mines (Case and Sebastien. 1989), and in lung tissues of miners (Stayner et al. 1996). The available data indicate there are higher levels of amphibole contamination in Thetford (3.7%) than at Asbestos (0.6%). However, because these estimates are based on measurements in ambient air rather than workplace air, the values are quite uncertain. Consequently, in the absence of other data, the uncertainty distribution for f_{amph} for Asbestos Mines and the Asbestos factory are taken to be:

PDF(f_{amph}) ~ TRI(0.002, 0.006, 0.018)

The uncertainty distribution for f_{amph} for Thetford Mines is taken to be:

$$PDF(f_{amph}) \sim TRI(0.012, 0.037, 0.11)$$

Uncertainty in Particle Size Data for Chrysotile

Of the TEM data sets available (see Appendix B), 11 are based on chrysotile asbestos. Two of these are derived from samples collected from Quebec mines, although which mines are not specified. The two data sets differ by operation as mining and bagging, so they were combined to represent both the mines and mills of Quebec. Since the TEM data is most likely derived from mines included in the epidemiology studies by McDonald et al. (1993) and Liddell et al. (1997), the uncertainty in f_{size} for chrysotile is low for each cohort, and is modeled as follows:

$$PDF(f_{size[chrysotile]}) \sim TRI(0.8, 1, 1.2)$$

Uncertainty in Particle Size Data for Amphibole

Amphibole (tremolite) contamination has been documented in chrysotile ores in general, from the ores around the Quebec mines, and in the lung tissues of workers in the mines and mills of these locations. Of the TEM data sets available (see Appendix B), 18 are based on amphibole asbestos, and one data set (from Dement and Harris 1979) is based on tremolite asbestos. This is from the talc production industry, and includes mining and milling operations. This TEM data set is applied to the Quebec epidemiology studies. Because the TEM set matches on amphibole type and is based on a similar industry, the uncertainty in f_{size} for amphibole is determined to be low, and is modeled as follows:

$$PDF(f_{size[amphibole]}) \sim TRI(0.8, 1.0, 1.2)$$

Figure A6-1. Lung Cancer Data for the Mine in Asbestos, Quebec

CE (mppcf-yr)		CE (PCM f/cc-yr)	Observed Deaths (a)	Expected Deaths (d)	SMR (a)	Relative Risk (e)		
Range (a)	Mean (b)	Mean (c)				Pt. Est. (e)	5% LB	95% UB
<30	15	54.6	61	40.9	1.5	1.5	1.2	1.8
30-100	65	236.6	28	21.7	1.3	1.3	0.9	1.7
100-300	200	728	22	16.2	1.4	1.4	0.9	1.9
>=300	500	1820	22	14.2	1.6	1.6	1.1	2.2

a) Data reported in Table 5 (McDonald et al. 1993).

b) Calculated as the midpoint of the reported range of CE10, except for the highest exposure group which has an unbounded range (5/3*lower bound).

c) A conversion factor equal to 3.64 is reported for this cohort in Gibbs and Lachance 1994.

d) Calculated value (observed deaths/relative risk).

e) SMR reported as proportions of the expected mortality rather than as percentages of it, therefore relative risk is essentially equal to SMR.

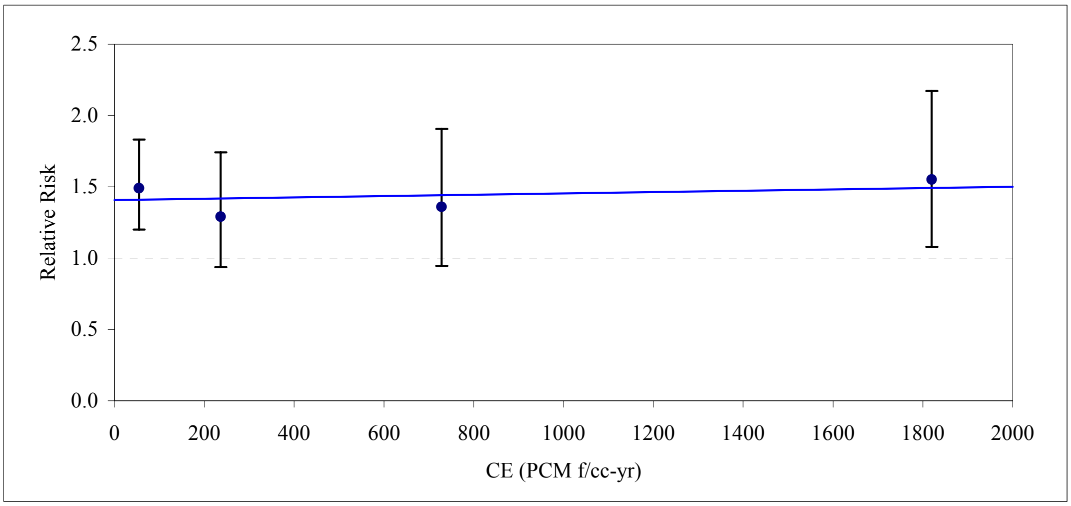


Figure A6-2. Lung Cancer Data for the Mines in Thetford, Quebec

CE (mppcf-yr)		CE (PCM f/cc-yr)	Observed	Expected	SMR(a)	Relative Risk		
Range (a)	Mean (b)	Mean (c)	Deaths (a)	Deaths (d)		Pt. Est. (e)	5% LB	95% UB
<30	15	54.6	37	36.6	1.0	1.0	0.8	1.3
30-100	65	236.6	36	20.8	1.7	1.7	1.3	2.3
100-300	200	728	28	26.7	1.1	1.1	0.8	1.4
>=300	500	1820	54	28.6	1.9	1.9	1.5	2.4

a) Data reported in Table 5 (McDonald et al. 1993).

b) Calculated as the midpoint of the reported range, except for the highest exposure group which has an unbounded range (5/3*lower bound).

c) A conversion factor equal to 3.64 is reported for this cohort in Gibbs and Lachance 1994.

d) Calculated value (observed deaths/relative risk).

e) SMR reported as proportions of the expected mortality rather than as percentages of it, therefore relative risk is essentially equal to SMR.

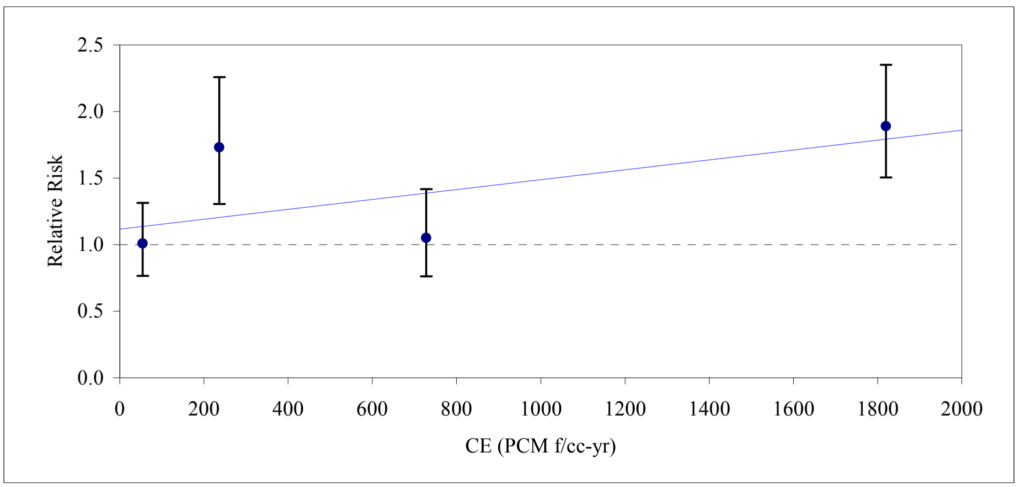


Figure A6-3. Lung Cancer Data for the Factory in Asbestos, Quebec

CE (mppcf-yr)		CE (PCM f/cc-yr)	Observed Deaths (a)	Expected Deaths (d)	SMR(a)	Relative Risk (e)		
Range	Mean	Mean				Pt. Est. (e)	5% LB	95% UB
<30	15	54.6	11	10.5	1.1	1.1	0.6	1.7
30-100	65	236.6	5	4.5	1.1	1.1	0.5	2.2
100-300	200	728	2	2.8	0.7	0.7	0.2	2.0
>=300	500	1820	4	0.6	7	7	2.9	14.8

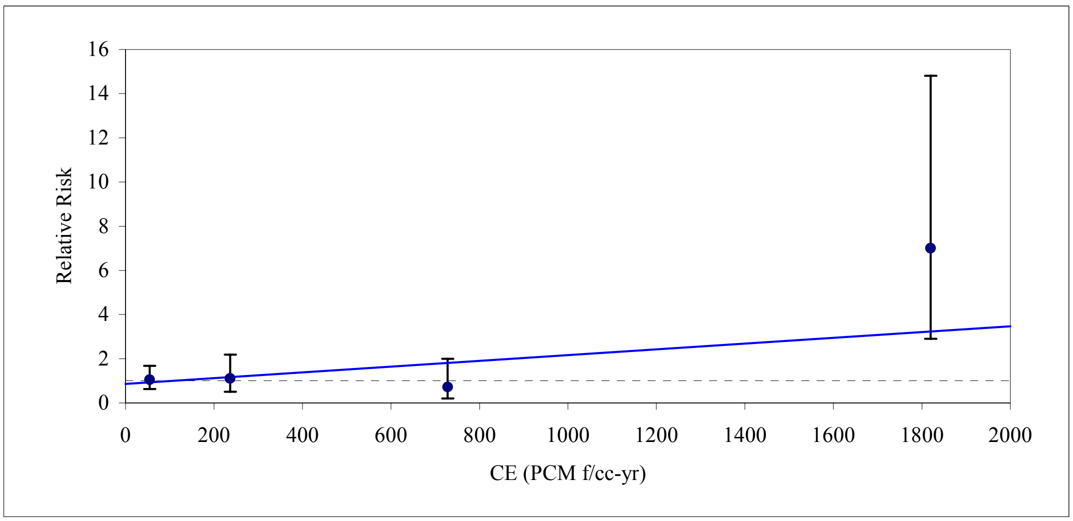
a) Data reported in Table 5 (McDonald et al. 1993).

b) Calculated as the midpoint of the reported range of CE10, except for the highest exposure group which has an unbounded range (5/3*lower bound).

c) A conversion factor equal to 3.64 is reported for this cohort in Gibbs and Lachance 1994.

d) Calculated value (observed deaths/relative risk).

e) SMR reported as proportions of the expected mortality rather than as percentages of it, therefore relative risk is essentially equal to SMR.



A7. Pennsylvania Textile Facility

References

Primary: McDonald, A., Fry, J., Woolley, A., and McDonald, J. (1982). Dust exposure and mortality in an American factory using chrysotile, amosite, and crocidolite in mainly textile manufacture. *British Journal of Industrial Medicine*, **39**: 368-374.

Other: Robinson, C., Lemen, R., and Wagoner, J. (1979). Mortality patterns 1940-1975 among workers employed in an asbestos textile friction and packing products manufacturing facility. In: Lemen, R., Dement, J., eds. *Dusts and Diseases.* Park Forest South, Illinois: Pathotox Publishers, Inc, pp. 131-143.

Mancuso, T., and Et Attar, A. (1967). Mortality pattern in a cohort of asbestos workers. *J. Occup. Med.* **9**:147-162.

Study Description

Location and Facility Description

The plant is located in a rural area near Lancaster, Pennsylvania. It began producing a variety of asbestos containing materials in the early 1900s. This plant primarily produced asbestos-based textiles, but also friction products and packings, many of which were made from the asbestos-containing textile products. Raw asbestos received at the plant was cleaned, opened, carded, spun, and wound to form cloth or tape. In addition, raw asbestos was blended with resin-binding ingredients for making friction products. Insulation blankets were produced from 1924 onward, although the manufacturing of insulation mattresses and filter cloth was transferred to another building from 1925 to 1931. After 1931, the other building was turned into a warehouse, and the production of cloth and mattresses was returned to the main plant.

Conditions in the plant were reported to be very dusty in the 1920s and 1930s. Beginning about 1930, some steps were taken to reduce dust levels, including wetting, improved handling, and ventilation hoods. By 1939, exhaust ventilation was installed. Thereafter, improvements in industrial hygiene were gradual (McDonald et al. 1982).

Asbestos Type

About 3,000 to 6,000 tons of chrysotile, obtained mostly from Canada and Rhodesia, were processed annually at the plant. Chrysotile was used in all departments of the plant including textile, friction and packing departments. Crocidolite and amosite were used from 1924 onward for making insulation blankets, equipment for chemical factories and paper mills, and filter materials. Crocidolite packing material was also produced. Much of the crocidolite was imported as yarn from England, but about 3-5 tons of raw crocidolite was processed annually. During 1942-1945, amosite insulation blankets were produced in large quantities for the U.S. Navy.

Fraction Amphibole

Chrysotile constituted over 99% of the asbestos used per year (5000-6000 tons/yr) except during the war years (Robinson et al. 1979). Between 1942 and 1945, use of amosite increased from < 1% to approximately 5% (375 tons/yr) of the total quantity of asbestos used. After the war, amosite usage decreased to < 1% (Robinson et al. 1979). Crocidolite usage was always < 1% (about 7,500 lbs/yr). Based on these data, the long-term average fraction amphibole is estimated to be about 1%.

Cohort Description and Follow-up

The cohort consisted of men and women employed for at least 1 month prior to 1959 who had a valid record with the Social Security Administration (SSA). The cohort fell into two groups that ultimately were combined: 1) those workers first employed after 1937, and 2) those workers employed before 1937. In all, 4,137 men and 998 women met the cohort criteria. Data for the females in the cohort are not presented in McDonald et al. (1982). The total number of person-years for this cohort is not reported.

Follow-up occurred through December 31, 1977. Survival status was obtained through local inquiries and information on deaths provided by the SSA. Three percent of the men (113 men) could not be traced. Of the 4,024 men followed through 1977, 1,400 men (35%) had died. Eight of these men were excluded from the analysis because of insufficient information on age. On average, men in this cohort began work around age 29 and were employed for 9 years.

Determination of Cause of Death and Diagnosis of Lung Cancer/Mesothelioma Cases

Cause of death was ascertained from copies of death certificates obtained from state offices or from the country where the death occurred. These were coded according to the seventh revision of the International Classification of Disease (ICD) by a single qualified nosologist. Of the 1,392 male deaths included in the analysis, death certificates were obtained for 1,354 (97%). For two male deaths where a certificate was unavailable, the cause of death was ascertained from other unspecified sources.

Reference Population

Mortality experience was compared with that expected based on Pennsylvania rates.

Estimating Exposure Concentration

Data on dust levels in the plant were available from several sources, including surveys conducted by the Metropolitan Life Insurance Company during the period 1930-1939, Public Health Service surveys conducted during 1967 and 1970, and company measurements made routinely from 1956 onward (McDonald et al. 1982). All environmental measurements made through 1967 were collected by midget impinger. It is assumed that the membrane filter method was used after this period, although the authors do not address the method used after 1967. The average dust concentration for this cohort was reported by McDonald et al. (1982) to be 1.84 mpcf. Dust measurements were used to estimate dust concentration levels by department and year in units of mppcf. The authors noted that this method of estimating concentration does not take into account certain additional exposures which may have been quite short but intense (e.g., daily "blowing down" and whipping of burlap bags in the dust house). No site-specific conversion factor was reported for this plant.

Estimating Cumulative Exposure

Cumulative exposures were estimated from employment histories based on age at start, duration of employment, and department. The main departments were categorized by manufacturing products as: textiles, friction products, packings and gaskets, and maintenance.

Smoking Data

Smoking histories of workers had been recorded starting in 1978. For men born in 1910-1919, the fraction of never smokers was 25%. Because this is based on only 36 workers, the authors stated that no firm conclusions could be drawn.

Lung Cancer Results

Table 5 in McDonald et al. (1982) report mortality from respiratory cancer (ICD 162-164; ICD-7 includes cancer of the trachea, bronchus, and lung, cancer of the pleura, and cancer of "other respiratory sites") as a function of cumulative exposure to dust (mppcf), lagged by 10 years, for workers who survived at least 20 years from the date of first employment. In the absence of a site-specific conversion factor, the default factor of 3 PCM f/cc per mppcf was used to convert from dust levels to asbestos levels (Appendix C). The results are shown in Figure A7-1. As seen, lung cancer mortality in this cohort exhibited a clear upward exposure-response trend.

In addition, as seen in Figure A7-1, relative risks of lung cancer are below 1 for the first two exposure groups in this cohort, suggesting that smoking prevalence may have been lower than in the reference population. However, data on smoking prevalence are too limited to evaluate this (McDonald et al 1982).

Mesothelioma Results

A diagnosis of mesothelioma was specified on 14 death certificates occurring between 1960 and 1975 (ten pleural and four peritoneal). One of these deaths (in 1960) occurred 16 years after first exposure, and the remaining 13 occurred 25 to 53 years after first employment. Two of these deaths were coded as "malignant neoplasms of other and unspecified sites" (ICD 199). This code was also assigned to an additional thirty deaths that occurred 15 years after first employment. The diagnosis reported on death certificates for most of these was consistent with an unrecognized peritoneal mesothelioma, but additional independent confirmation was not conducted.

The 14 deaths for which a diagnosis of mesothelioma was specified on death certificates were included in the OSWER mesothelioma data set. The number of person years of observation were not reported, but may be estimated from total (all-cause) mortality data stratified by age at death, as described in Appendix A, Attachment A-1. Likewise, values of C·Q for each group were not reported, but may be estimated by assuming that the average value of T (time since first exposure) is equal to the midpoint of the age bin minus the average age at first exposure, and combining this with the average value of d (exposure duration) and the average value of C (concentration). These data were combined into one group as described in Attachment A-1 and the resulting values are shown in Figure A7-2.

Uncertainty and Bias Characterization

Appendix C discusses the primary sources of uncertainty in epidemiological studies of cancer risk from asbestos exposure in the workplace and describes the methods used in this document for characterizing the uncertainty. The following sections discuss the uncertainty characterization and issues of potential bias for this study.

Uncertainty Due to Measurement Error

As described in Section 3.1 of Appendix C, all estimates of concentration levels of asbestos in the workplace are uncertain due to the combination of sampling error and analytical error. These measurements are usually averaged according to job or work area, often stratified by time. For this study, McDonald et al. (1982) report mean concentrations as a function of time period and operation (see Table 2 in the original report). The magnitude of the uncertainty in the reported mean value for each job/time category (which is used to compute cumulative exposure) is a function of a) the number of samples used to compute the mean, b) the between-sample variability, and c) the nature of the underlying distribution. However, the authors do not provide information on the number of samples collected, or on the degree of between-sample variability. Therefore, in the absence of data, the default assumption described in Appendix C is applied to this study to account for measurement error, and is characterized as:

PDF(measurement error) ~ TRI(0.6, 1, 1.5)

Uncertainty in Mean Values for Lung Cancer Exposure Groups

The authors report CE10 values as ranges for the five exposure groups. For the four exposure groups with bounded ranges, the mid-point of the range is taken as the point estimate. As discussed in Appendix C, this point estimate is an uncertain estimate of the true mean, and the uncertainty is characterized as follows:

PDF(exposure, bounded) ~ TRI(Min/Mid, 1, Max/Mid)

For the highest exposure group with an unbounded range (CE $\geq$ 80 f/cc-yr), the point estimate and uncertainty is modeled as:

PDF(exposure, unbounded) ~ TRI(1, 5/3, 3)

Uncertainty in Conversion Factor (CF) from Dust Data (mppcf) to PCM f/cc

At this plant, workplace air measurements were collected from 1956 to 1967 using midget impingers. Air measurements are available for this plant through 1970. McDonald et al. (1982) state that up until 1967 midget impingers were used. From this statement, it is assumed that the membrane filter method was used after this period although this is not explicitly stated. As described in Appendix C, since a site-specific conversion factor is not available for this plant, a default value of 3.0 is applied and is characterized by:

PDF(conversion factor) ~ TRI(0.33, 1, 3.33)

Uncertainty Due to Unmeasured Short-Duration High Exposures

As noted above, the authors stated that dust measurements collected in the workplace did not capture short-term but high level exposures that may have occurred during daily "blowing down" and whipping of burlap bags in the dust house. While this almost certainly results in some degree of under-estimation of cumulative exposure for some individuals, it is very difficult to judge a) what fraction of the cohort would have been exposed from this activity, and b) the magnitude of the error in cumulative exposure that might result. For example, if the job was always performed by the same individuals, their cumulative exposures would be substantially underestimated, but the person-years of observation for these individuals would constitute only a small fraction of the total observations. Conversely, if the job was rotated among many individuals, then the magnitude of the error in the cumulative exposure for each person-year would be small, and would likely result in only a small number of person years being re-classified from one exposure bin to the next highest bin. In the absence of data, and recognizing that the authors of the study did not attempt to adjust for these exposures, no added uncertainty is added in this analysis to account for this underestimation. Note that failure to account for underestimation of exposure, if significant, would tend to result in an overestimation of potency.

Uncertainty in the Use of Stationary Rather Than Personal Air Monitors

McDonald et al. (1982) do not report the use of personal air monitors. In the absence of knowledge, it is assumed the measures were collected using stationary monitors. As discussed in Appendix C, use of stationary monitors may tend to underestimate the true exposure level of workers, especially those engaged in activities that actively disturb asbestos-containing materials or dusts. Based on available data on the ratio of particulate concentrations measured using personal to stationary monitors at various locations, the uncertainty attributable to this source may be characterized as:

PDF(personal vs. stationary) ~ BETA(2 ,20 , 0.9, 10)

Uncertainty in Temporal Representativeness

As mentioned previously, surveys of the workplace environment were conducted from 1930-1939, and 1967-1970. Beginning in 1956, routine measurements were conducted by the company. The Pennsylvania plant opened in the 1900's and the cohort defined by McDonald et al. (1982) included employees hired prior to 1959. Anecdotal information on conditions in the 1920's and 30's was used to estimate early exposures. As discussed in Appendix C, when available data is moderately representative over time, uncertainty in this case is considered to be medium and is characterized as follows:

PDF(temporal representativeness) ~ TRI(0.8, 1, 1.2)

Bias Correction Factor in Lung Cancer Data Reported as CE Rather Than CE10

McDonald et al. (1982) report lung cancer mortality stratified by cumulative exposure lagged by ten years. Therefore no BCF is required for this cohort.

Uncertainty in Mesothelioma Data

As discussed in Attachment 1, two approximations were necessary in order in order to utilize the data from this study in the quantitative mesothelioma model fitting exercise. First, it was necessary to estimate the number of person-years of observation from all-cause mortality data, and second, it was necessary to estimate the value of cumulative exposure (C·Q) from data on the average age at first exposure, the average exposure duration, and the average exposure concentration. As described in Attachment 1, the combined uncertainty associated with these approximations may be characterized as follows:

$PDF(\text{combined effect of approximations}) \sim TRI\ (0.4, 1, 2.5)$

Uncertainty in Fraction Amphibole

As noted above, the average amount of amphibole (amosite and crocidolite) used in the plant was generally < 1%, but reached a level of about 5% during World War II (Robinson et al. 1979). Based on this, an estimate of the long-term average is about 1%. Because the estimate of 1% amphibole is based on reported quantities of asbestos used, and because the value is time variable, uncertainty around the point estimate is moderately large. Based on professional judgment, the uncertainty distribution is characterized as:

$PDF(f_{amph}) \sim TRI(0.005, 0.010, 0.02)$

Uncertainty in Particle Size Data for Chrysotile

As mentioned above, this plant used primarily chrysotile asbestos. The plant produced mainly textiles, but also manufactured friction products and insulation blankets. Of the TEM data sets available (see Appendix B), 11 are based on chrysotile asbestos. Three of these data sets each correspond to the textile and friction product industries. None of the data sets correspond to the use of chrysotile asbestos in the production of insulation. The textile data sets differ by operation as preparation, twisting, and weaving. The friction product data sets also differ by operation as mixing, forming, and finishing. These operations were all performed at the Pennsylvania plant, and there is no basis to select one TEM data set over the other. Therefore, the six chrysotile data sets based on the textile and friction product industries were combined. Since the assigned TEM data sets match on asbestos type and industry, the uncertainty in f_{size} for chrysotile is determined to be low, and is modeled as follows:

$PDF(f_{size[chrysotile]}) \sim TRI(0.8, 1, 1.2)$

Uncertainty in Particle Size Data for Amphibole

Both crocidolite and amosite asbestos were used in this factory. The uses of crocidolite are not detailed by the authors, but amosite was used mainly for making fire-retardant blankets during WWII. Of the TEM data sets available (see Appendix B), 18 are based on amphibole asbestos. Eight of these data sets are based on crocidolite asbestos, and five are based on amosite asbestos, and none of them are based on the textile or friction product industry. Of the TEM data sets based on crocidolite asbestos, five are from the mining industry and three are from the cement manufacturing industry. Two of the amosite data sets are based on the mining industry, and three are based on the manufacturing of pipe insulation. There is no basis to choose one crocidolite TEM data set over the other, but in the case of the amosite data sets, those based on insulation manufacturing are more applicable to this study since this plant used amosite to produce insulation blankets. Therefore, the eight TEM crocidolite data sets were combined with the three amosite insulation data sets and applied to this study. As described in Appendix C, if TEM data sets are available that match on mineral form but not on industry, the uncertainty in f_{size} for amphibole is determined to be medium, and is modeled as follows:

$$PDF(f_{size[amphibole]}) \sim TRI(0.5, 1.0, 1.5)$$

Figure A7-1. Raw Lung Cancer Data for the Pennsylvania Plant

CE_{10} (mppcf-yr)		CE_{10} (PCM f/cc-yr)	Observed Deaths (a)	Expected Deaths (d)	SMR (a)	Relative Risk		
Range (a)	Mean (b)	Mean (c)				Pt. Est. (e)	5% LB	95% UB
< 10	5	15	21	31.4	66.9	0.7	0.5	0.9
10-20	15	45	5	6.0	83.6	0.8	0.4	1.6
20-40	30	90	10	6.4	156	1.6	0.9	2.5
40-80	50	150	6	3.8	160	1.6	0.8	3.0
>=80	133.3	400	11	2.6	416.1	4.2	2.5	6.7

a) Data reported in Table 5 (McDonald et al. 1982).

b) Calculated as the midpoint of the reported range of CE10, except for the highest exposure group which has an unbounded range. The point estimate is assigned a value = 5/3*lower bound.

c) A site-specific conversion factor is not available for this cohort; assume the default conversion factor of 3.0 for the range of conversion factors observed among available studies (see Appendix C for further explanation).

d) Calculated value (observed deaths/relative risk).

e) Relative risk equal to SMR/100.

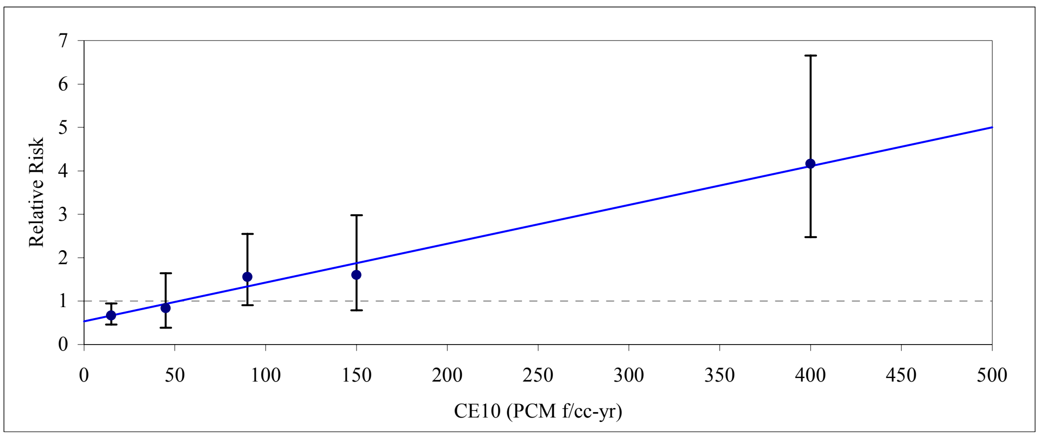


Figure A7-2. Raw Mesothelioma Data for the Pennsylvania Plant

Age Range		Avg Age at Start (a)	Yrs since start	D (yrs) (a)	Q (yrs^3)	Conc (a,b)		Reconstruction of PY (c)		
Range	Pt. Est.					mppcf	f/cc	Observed Deaths (d)	SMR (e)	PY
29-44	36.5	28.92	7.54	9.18	0.00	2.32	6.96	191	1.090	61110
45-64	54.5	28.92	25.58	9.18	3519.69	2.32	6.96	667	1.090	41797
>= 65	75	28.92	46.08	9.18	27502.62	2.32	6.96	534	1.090	7767

a) Observed values reported in Table 3 (McDonald et al. 1982).

b) Dust concentrations were measured by impinger. An assumed conversion factor of 3 was applied to convert to PCM (f/cc).

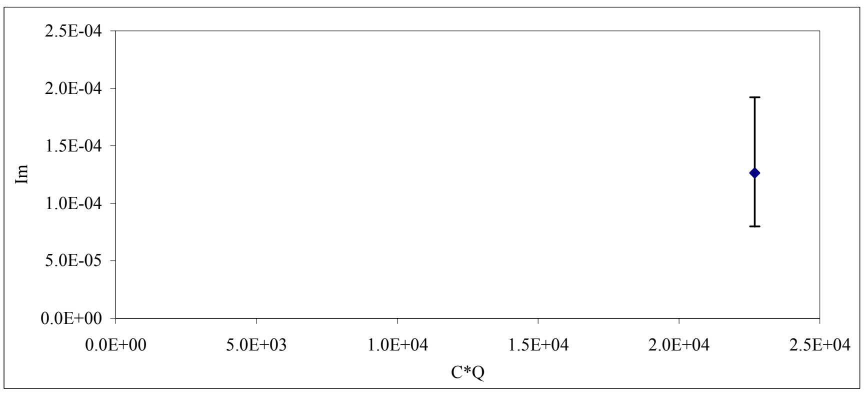
c) Person-years were reconstructed based on the method presented in Attachment A-1.

d) Observed deaths from all causes for the given age groups are reported in Table 1 (McDonald et al. 1982).

e) SMR for all cause deaths for the complete cohort reported in Table 4 (McDonald et al. 1982). The same value is assumed to apply to all groups.

C*Q (f)	PY (g)	Observed Cases	Incidence (Im)	Uncertainty Bounds	
				5% LB	95% UB
22685	110673	14	1.26E-04	8.0E-05	1.9E-04

f) Calculated as the PY weighted average as described in Appendix C.
g) Calculated as the sum of the reconstructed PY across all three age bins.



A8. Connecticut Friction Products Plant

References

Primary: McDonald, A., Fry, J., Woolley, A., and McDonald, J. (1984). Dust exposure and mortality in an American chrysotile asbestos friction products plant. *British Journal of Industrial Medicine*, **41**: 151-157.

Other: McDonald, A., and Fry, J. (1982). Mesothelioma and fibre type in three American asbestos factories; preliminary report. *Scandinavian Journal of Work and Environmental Health*, 8(suppl): 53-58.

Teta MJ, Lewinsohn HC, Meigs JW, Vidone RA, Mowad LZ, Flannery JT. Mesothelioma in Connecticut, 1955-1977. J. Occup. Med. 25:749-756.

Study Description

Location and Facility Description

The plant located in Connecticut began operation in 1913, manufacturing asbestos-based friction products. Initially, processes at this plant involved the production of compressed rubber asbestos sheet packing material, and the production of mill board on wet machines for use in clutch facings and brake linings. A dry process, beginning in the late 1930s and ending in 1970, involved the production of dry molded and roll extruded wire back brake linings. Beginning in the 1940s a large volume of friction materials for automatic transmissions were produced.

Asbestos Type

Only chrysotile asbestos, mainly from Canada, was used until 1957, when some anthophyllite was also used in making paper discs and bands. No information was provided on the amounts of anthophyllite used. Also, a small amount of crocidolite (about 400 pounds) was used experimentally between 1964 and 1972.

Fraction Amphibole

Data provided in the study report are not adequate to calculate the average fraction amphibole for this cohort. The amount of crocidolite used is assumed to be negligible.

However, the amount of anthophyllite used is likely not negligible. In the absence of additional data, it is assumed that the amount of anthophyllite used in the manufacture of paper discs and bands is about 10% of the total asbestos, and that this product constituted no more than 10% of the total asbestos products from this plant. Thus, when anthophyllite was in use, the fraction amphibole would be about 1%. Since anthophyllite was not used continuously, but only after 1957, the long-term average fraction must be lower than this, so a value of 0.5% is assumed.

Cohort Description and Follow-up

The cohort was defined as any worker who had been employed at the plant for at least 1 month before 1959, and who had a social security number and name that matched data in the United States social security files. Based on this definition, the cohort consisted on 4,028 men and 931 women. The authors chose to exclude workers that had worked at a nearby asbestos textile plant that closed in 1939, and to exclude the women workers. This reduced the size of the cohort to 3,641 men. The total number of person-years for this cohort is not reported.

This cohort was followed through December 31, 1977. Approximately 3% of the men were lost to follow-up. Of the 3,513 men for which vital status was established, 1,267 (36%) had died by the end of follow-up. On average, men in this cohort began work around age 30 and were employed for 8 years.

Determination of Cause of Death and Diagnosis of Lung Cancer/Mesothelioma Cases

Vital status was determined from death certificates by a qualified nosologist using the 7^{th} revision of the International Classification of Diseases. Death certificates were obtained for 1,228 (96.9%) of these men. For the deaths without certificates (3%), cause was ascertained from other unspecified sources.

Reference Population

For the mortality analysis, age, sex, race, and year specific death rates for Connecticut were used for reference.

Estimating Exposure Concentration

Information on dust levels from impinger measurements (mppcf) was available for the years 1930, 1935, 1936, and 1939. There was little other exposure information available until the 1970s, when membrane filter sampling and analysis by PCM began. No site-specific data on the correlation between mppcf and PCM f/cc were available. Estimates of average dust concentrations by process and period were made by an industrial hygienist in September 1980 based on available information from plant records and interviews with long term employees.

Estimating Cumulative Exposure

Dust levels in each department as a function of calendar year were estimated from available measurements and from information provided by long-term employees about relative levels of dust in different areas and different times. These estimated values (presented in Table 2 of McDonald et al. 1984) ranged from 1-25 mppcf in 1930-39, decreasing to 0.1-6 mppcf by 1960-69.

Employee records were used to obtain information on individual work histories from this plant. Work histories included the department in which a person worked, although the specific job or process was seldom provided. To account for this, cumulative exposure estimates were made for departments rather than processes. The level of dust produced by different processes varied within a department. In general, few workers were employed in the extremely dusty processes within a department, while many more workers were employed in the other less dusty processes. McDonald et al. (1984) attempted to account for the more dusty processes, recognizing that in doing so exposure estimates may have been overestimated for most employees in these departments and underestimated for a few.

Smoking Data

McDonald et al. (1982) stated that the prevalence of non-smokers in this cohort was 16%.

Lung Cancer Results

Table 5 in McDonald et al. (1984) report mortality from respiratory cancer (ICD 162-164; ICD-7 includes cancer of the trachea, bronchus, and lung, cancer of the pleura, and cancer of "other respiratory sites") as a function of cumulative exposure to dust (mppcf), for workers who survived at least 20 years from the date of first employment. In the absence of a site-specific conversion factor, the default factor of 3 PCM f/cc per mppcf was used to convert from dust levels to asbestos levels (Appendix C). The results are shown in Figure A8-1. Risk from lung cancer was the highest for men in the lowest exposure category and lowest for men in the highest exposure category, and the overall exposure-response trend was negative. This pattern was also observed when comparing relative risk of respiratory cancer and duration of employment, with highest risk for men exposed for < 1 year. The authors speculated that some selective process common in industry may have lead to the employment of men of relatively poor health. Also, company records suggest a pattern of those short-term employees working in other hazardous industries before or after their employment at the asbestos plant. It is important to note that the measure of cumulative exposure reported by the authors was not lagged by 10 years, which will tend to result in a lower slope of the exposure-response curve than if values lagged by 10 years were used.

Mesothelioma Results

McDonald et al. (1984) did not find any cases of mesothelioma in this cohort. The number of person years of observation were not reported, but may be estimated from total (all-cause) mortality data stratified by age at death, as described in Appendix A, Attachment A-1. Likewise, values of C·Q for each group were not reported, but may be estimated by assuming that the average value of T (time since first exposure) is equal to the midpoint of the age bin minus the average age at first exposure, and combining this with the average value of d (exposure duration) and the average value of C (concentration). These data were combined into one group as described in Attachment A-1 and the resulting values are shown in Figure A8-2.

Although the original study (McDonald et al. 1984) did not identify any deaths from mesothelioma in this workplace, a review of the State cancer registry by Teta et al. (1983) revealed that three Connecticut residents who died of mesothelioma were employed by the same friction products company. One of these employees had amphibole exposures at another asbestos plant. A pathology review indicated that one of these cases was a probable pleural mesothelioma in a woman with 5 years of exposure; the other case was a peritoneal mesothelioma in a woman who also had asbestosis and worked as a clerk for 30 years.

Uncertainty Characterization

Appendix C discusses the primary sources of uncertainty in epidemiological studies of cancer risk from asbestos exposure in the workplace and describes the methods used in this document for characterizing the uncertainty. The following sections discuss the uncertainty characterization and issues of potential bias for this study.

Uncertainty Due to Measurement Error

As described in Section 3.1 of Appendix C, all estimates of concentration levels of asbestos in the workplace are uncertain due to the combination of sampling error and analytical error. These measurements are usually averaged according to job or work area, often stratified by time. For this study, McDonald et al. (1984) report mean concentrations as a function of time period and operation (see Table 2 in the original report). The magnitude of the uncertainty in the reported mean value for each job/time category (which is used to compute cumulative exposure) is a function of a) the number of samples used to compute the mean, b) the between-sample variability, and c) the nature of the underlying distribution. However, the authors do not provide information on the number of samples collected, or on the degree of between-sample variability.

Therefore, in the absence of data, the default assumption described in Appendix C is applied to this study to account for measurement error, and is characterized as:

PDF(measurement error) ~ TRI(0.6, 1, 1.5)

Uncertainty in Mean Values for Lung Cancer Exposure Groups

The authors report cumulative exposure values for lung cancer as ranges for five exposure groups. For the four exposure groups with bounded ranges, the mid-point of the range is taken as the point estimate. As discussed in Appendix C, this point estimate is an uncertain estimate of the true mean, and the uncertainty is characterized as follows:

PDF(exposure, bounded) ~ TRI(Min/Mid, 1, Max/Mid)

For the highest exposure group with an unbounded range ($\geq$ 80 f/cc-yr), the point estimate and uncertainty is modeled as:

PDF(exposure, unbounded) ~ TRI(1, 5/3, 3)

Uncertainty in Conversion Factor (CF) from Dust Data (mppcf) to PCM f/cc

At this plant, workplace air measurements were collected using midget impingers prior to 1970, and the membrane filter method was used subsequently. McDonald et al. (1984) did not attempt to compute a conversion factor due to the large amount of work required to convert particle estimates to fiber measurements. As described in Appendix C, since a site-specific conversion factor is not available for this plant, a default value of 3.0 is applied and is characterized by:

PDF(conversion factor) ~ TRI(0.33, 1, 3.33)

Uncertainty in the Use of Stationary Rather Than Personal Air Monitors

Although the authors do not explicitly state the nature of the air monitors in the plant, it is assumed available data were collected using stationary monitors. As discussed in Appendix C, use of stationary monitors may tend to underestimate the true exposure level of workers, especially those engaged in activities that actively disturb asbestos-containing materials or dusts. Based on available data on the ratio of particulate concentrations measured using personal to stationary monitors at various locations, the uncertainty attributable to this source may be characterized as:

PDF(personal vs. stationary) ~ BETA(2, 20, 0.9, 10)

Uncertainty in Temporal Representativeness

As mentioned previously, the data used to estimate concentration values in the Connecticut factory, which began operations in 1913, were primarily based on surveys conducted at the plant by the Metropolitan Life Insurance Company for the years 1930, 1935, 1936, and 1939. Measurements are lacking for the period between 1940 and 1970. Estimates of workplace air for this period were mainly based on anecdotal information from long-term employees and factory records. As discussed in Appendix C, when data are missing for a significant portion of the exposure period and has to be extrapolated from other sources, the uncertainty associated with the temporal representativeness is considered to be high, and is characterized as follows:

PDF(temporal representativeness) ~ TRI(0.5, 1, 1.5)

Bias Correction Factor for Lung cancer Data Reported as CE Rather Than CE10

This study reports cumulative exposure as CE rather than as CE10. As discussed in Appendix C, use of CE rather than CE10 tends to bias results low, with the magnitude depending on the duration of exposure, the length of follow-up, and whether or not early person years of observation were excluded. McDonald et al. (1984) reports the average duration of net service as 8.04 years. End of follow-up was in 1977 and the average time since last exposure was estimated to be 29 years. McDonald et al. (1984) report lung cancer data based on a latency period of 20 years. Based on this information, a BCF was assigned to this cohort as follows:

$$BCF \sim TRI(1, 1, 1)$$

Effectively, for this study the bias associated with reporting cumulative exposure as CE rather than CE10 is negligible. The BCF ~ 1.0, and therefore it is not necessary to apply any BCF to this study.

Uncertainty in Mesothelioma Data

As discussed in Attachment 1, two approximations were necessary in order in order to utilize the data from this study in the quantitative mesothelioma model fitting exercise. First, it was necessary to estimate the number of person-years of observation from all-cause mortality data, and second, it was necessary to estimate the value of cumulative exposure ($C \cdot Q$) from data on the average age at first exposure, the average exposure duration, and the average exposure concentration. As described in Attachment 1, the combined uncertainty associated with these approximations may be characterized as follows:

$$PDF(\text{combined effect of approximations}) \sim TRI\ (0.4, 1, 2.5)$$

Uncertainty in Fraction Amphibole

As noted above, the Connecticut plant used only chrysotile asbestos up until 1957. After this time, some anthophyllite was used in making paper disc bands, although the authors do not provide any information that allows for a quantitative estimate of the amount used. Based on the lack of information on the amount of amphibole used at this plant the uncertainty bounds around the point estimate of 0.5% are wide and are based on professional judgment only. The uncertainty distribution around the point estimate of f_{amph} is characterized as:

$$PDF(f_{amph}) \sim TRI(0.001, 0.005, 0.020)$$

Uncertainty in Particle Size Data for Chrysotile

As mentioned above, the friction product plant evaluated by this study used primarily chrysotile asbestos. Of the TEM data sets available (see Appendix B), 11 are based on chrysotile asbestos. Three of these data sets correspond to the friction product industry. These data sets differ by operation as mixing, forming, and finishing. These operations were all performed at the Connecticut plant, and there is no basis to select one TEM data set over the other. Therefore, the three chrysotile data sets based on the friction product industry were combined. Since the assigned TEM data sets match on asbestos type and industry, the uncertainty in f_{size} for chrysotile is determined to be low, and is modeled as follows:

$$PDF(f_{size[chrysotile]}) \sim TRI(0.8, 1, 1.2)$$

Uncertainty in Particle Size Data for Amphibole

At this plant, anthophyllite was used in making some friction products. Small amounts of crocidolite were used, but this is considered to be negligible. Of the TEM data sets available (see Appendix B), 18 are based on amphibole asbestos, and two of these are based on anthophyllite asbestos, although neither is from the friction product industry. Since there is no basis to prefer either of the anthophyllite data sets, both were combined and applied to this study. As described in Appendix C, if TEM data sets are available that match on mineral form but not on industry, the uncertainty in f_{size} for amphibole is determined to be medium, and is modeled as follows:

$$PDF(f_{size[amphibole]}) \sim TRI(0.5, 1.0, 1.5)$$

Figure A8-1. Raw Lung Cancer Data for the Connecticut Friction Products Plant

CE (mppcf-yr)		CE (PCM f/cc-yr)	Observed	Expected		Relative Risk		
Range (a)	Mean (b)	Mean (c)	Deaths (a)	Deaths (d)	SMR (a)	Pt. Est. (e)	5% LB	95% UB
< 10	5	15	55	32.9	167.4	1.7	1.3	2.1
10-20	15	45	6	5.9	101.7	1.0	0.5	1.9
20-40	30	90	5	4.7	105.4	1.1	0.5	2.1
40-80	60	180	6	3.7	162.8	1.6	0.8	3.0
>=80	133.3	400	1	1.8	55.2	0.6	0.1	2.2

a) Data reported in Table 5 (McDonald et al. 1984).

b) Calculated as the midpoint of the reported range of CE, except for the highest exposure group which has an unbounded range. The point estimate is assigned a value = 5/3*lower bound.

c) A site-specific conversion factor is not available for this cohort; assume the default conversion factor of 3.0 for the range of conversion factors observed among available studies (see Appendix C for further explanation).

d) Calculated value (observed deaths/relative risk).

e) Relative risk equal to SMR/100.

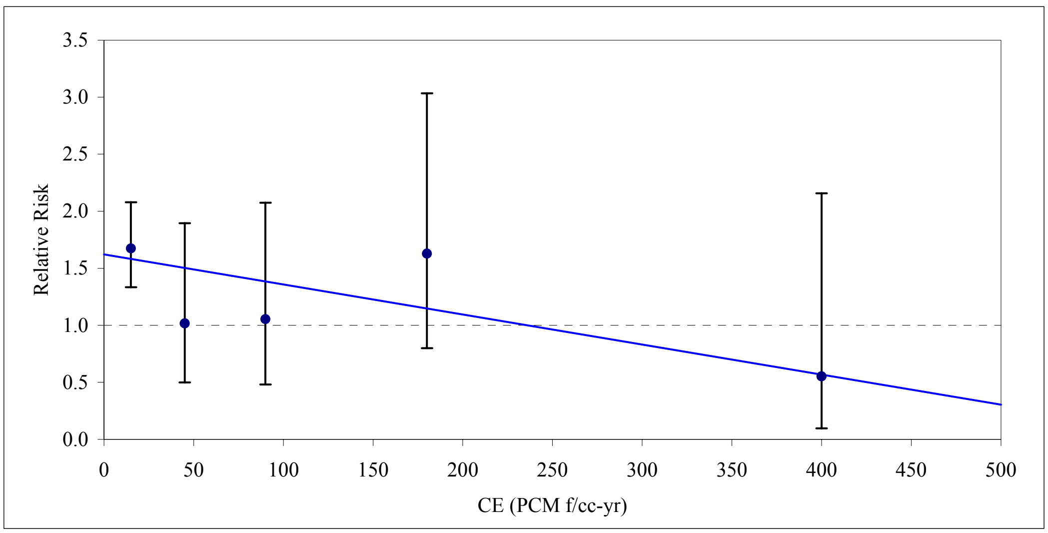


Figure A8-2. Raw Mesothelioma Data for the Connecticut Friction Products Plant

Age Range		Avg Age at Start (a)	Yrs since start	D (yrs) (a)	Q (yrs^3)	Conc (a,b)		Reconstruction of PY (c)		
Range	Pt. Est.					mppcf	f/cc	Observed Deaths (d)	SMR (e)	PY
31-44	37.5	30.95	6.53	8.04	0	1.84	5.52	139	1.085	36978
45-64	54.5	30.95	23.55	8.04	2321	1.84	5.52	616	1.085	38779
>= 65	75	30.95	44.05	8.04	21881	1.84	5.52	511	1.085	7466

a) Observed values reported in Table 3 (McDonald et al. 1984).

b) Dust concentrations were measured by impinger. An assumed conversion factor of 3 was applied to convert to PCM (f/cc).

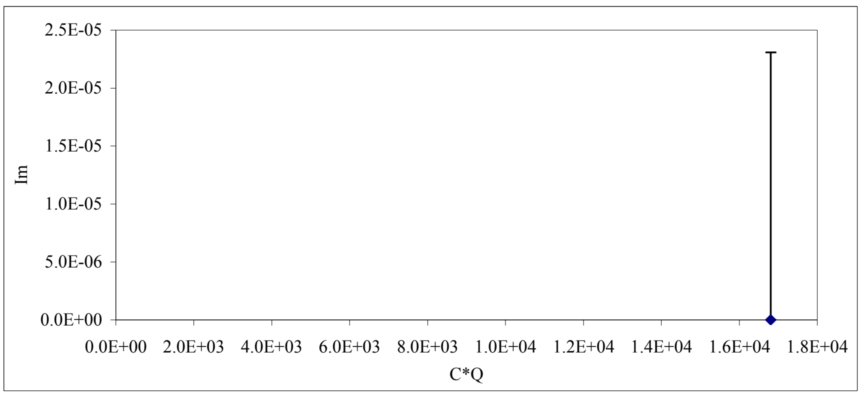
c) Person-years were reconstructed based on the method presented in Attachment A-1.

d) Observed deaths from all causes for the given age groups are reported in Table 1 (McDonald et al. 1984).

e) SMR for all cause deaths for the complete cohort reported in Table 4 (McDonald et al. 1984). The same value is assumed to apply to all groups.

C*Q (f)	PY (g)	Observed Cases	Incidence (Im)	Uncertainty Bounds	
				5% LB	95% UB
16805	83222.9	0	0.00E+00	2.4E-08	2.3E-05

f) Calculated as the PY weighted average as described in Appendix C.
g) Calculated as the sum of the reconstructed PY across all three age bins.



A9. British Textile Factory

References

Primary: Peto J, Doll R, Hermon C, Binns W, Clayton R, Goffe T. 1985. Relationship of mortality to measures of environmental asbestos pollution in an asbestos textile factory. Ann. Occup. Hygeine 29:305-355.

Other: Peto J, Doll R, Howard SV, Kinlen LJ, Lewinsohn HC. 1977. A mortality study among workers in an English asbestos factory. British J. Ind. Med. 34:169-173.

Peto J. 1980a. Lung Cancer Mortality in Relation to Measured Dust Levels in an Asbestos Textile Factory. In: Biological Effects of Mineral Fibres. Wagner JC (ed.). IARC Scientific Publications, pp. 829–836.

Peto J. 1980b. The Incidence of Pleural Mesothelioma in Chrysotile Asbestos Textile Workers. In: Biological Effects of Mineral Fibres. Wagner JC (ed.). IARC Scientific Publications. pp. 703–711. 1980b.

Peto J; Seidman H; Selikoff IJ. 1982. Mesothelioma Mortality in Asbestos Workers: Implications for Models of Carcinogenesis and Risk Assessment. British Journal of Cancer. 45:124–135.

Study Description

Location and Facility Description

The factory was located in Rochdale, England. It was established in 1855 to weave cotton, and began experimenting with asbestos in 1879 (Peto et al. 1985). Over the next 30 years, a variety of textile and non-textile asbestos products were developed. The company continued to grow, producing a wide range of asbestos-based products.

Asbestos Type

The textile works in the Rochdale factory has used chrysotile as the principal raw ingredient from the time it started asbestos operations until present times (Peto et al., 1985). Before 1965, most of the chrysotile was imported from Rhodesia, while after this time the source was primarily from Canada. No amosite was ever used for production purposes, although a very small amount (a few hundred pounds) were used for research in the early 1950s. Some crocidolite was used in manufacturing from 1932 to 1969. The total amount of crocidolite purchased over this 37-year time interval was about 10,300 tons, which was approximately 2.6% of the total amount of asbestos purchased over this same time period (Peto et al. 1985; Appendix A).

Fraction Amphibole

Based on the information above, the fraction amphibole in the workplace atmosphere was assumed to be 2.6%.

Cohort Description and Follow-up

The principal cohort evaluated consisted of two sub-groups: men who were first employed in 1933 or after, and who had completed at least five years of service before 1974, and a 1 in 10 sample of all men who began work in 1933 or after, without regard to the duration of service. The total number of men in both groups combined, after exclusions, was 3,211 (Peto et al. 1985). The total number of person-years included in the principal cohort was not reported.

Follow-up was carried out through June 30, 1983. Trace could not be completed for 140 men, and by the end of the follow-up period 44% (1,414 men) of the cohort had died.

Determination of Cause of Death and Diagnosis of Lung Cancer and Mesothelioma Cases

The National Health Service Register, factory records, and the national mesothelioma register were used to determine cause of death (Peto et al. 1985). All available diagnostic information on the mesothelioma cases was gathered, including microscopic evidence, histology, and other postmortem evidence, and evaluated by a mesothelioma expert (Richard Doll).

Reference Population

The mortality expected in the exposed groups was calculated by multiplying the person-years at risk by the corresponding sex, age and calendar-year specific mortality rates based on England and Wales combined (Peto et al. 1985).

Estimating Exposure Concentration

Measurements of the atmosphere in the workplace were made on a routine basis beginning about 1951. Initially (1951-1960), thermal precipitators were used and all particles, including fibers, were counted by dark field microscopy. Between 1961 and 1964, samples were still collected by thermal precipitator, but analysis was by light field microscopy, and only fibers longer than 5 um and with an aspect ratio of 3:1 or greater were counted. Beginning in 1965, samples were collected using the PCM membrane filter method. Based on regression analysis of paired samples analyzed by dark field microscopy (particles per mL) and by light field microscopy (fibers per mL), the authors found that 1 fiber = 35.3 particles. This corresponds to a conversion factor of 0.028 f/cc per particle per cc.

Estimating Cumulative Exposure

For each individual in the cohort, a detailed job history was compiled, including the section of the factory where he worked and the type of work performed. Concentration values (see above) were grouped into four different work areas, and all measurements from each area were averaged by year. Cumulative exposure of each individual was computed as the sum of the relevant yearly average values across years, allowing for a lag of five years.

Smoking Data

No systematic smoking history data exists for this cohort.

Lung Cancer Results

Lung cancer data for men with a minimum latency of 20 years after first employment are presented in Table 16 of Peto et al. (1985). These data are shown in Figure A9-1. As seen, an increasing trend in relative risk as a function of cumulative exposure was observed.

Mesothelioma Results

Table 8 of Peto et al. (1985) reports the number of mesothelioma cases in the cohort stratified according to duration of exposure (d) and years since first employment (T), along with the number of person-years of observation for each group. These data are sufficient to compute mesothelioma incidence (Im) and Q. However, the authors did not report the average exposure concentration (f/cc) for each group. Peto et al. (1977, Table 6) report concentration measurements taken over time from 1936 to 1972. These data are summarized below:

Year	1936	1941	1946	1951	1952	1956	1960	1961	1966	1971	1972	Mean
Conc (f/cc)	13.3	14.5	13.2	10.8	10.9	5.3	5.4	6.2	5.4	3.4	2.9	8.2

The average concentration as measured from 1936 – 1972 (8.2 f/cc) was used to compute cumulative exposure (C·Q) for mesothelioma as summarized in Figure A9-2.

Uncertainty and Bias Characterization

Appendix C discusses the primary sources of uncertainty in epidemiological studies of cancer risk from asbestos exposure in the workplace and describes the methods used in this document for characterizing the uncertainty. The following sections discuss the uncertainty characterization and issues of potential bias for this study.

Uncertainty Due to Measurement Error

As described in Section 3.1 of Appendix C, all estimates of concentration levels of asbestos in the workplace are uncertain due to the combination of sampling error and analytical error. These measurements are usually averaged according to job or work area, often stratified by time. For this study, Peto et al. (1977) report mean concentrations as a function of time period and operation (see Table 5 in the original report). The magnitude of the uncertainty in the reported mean value for each job/time category (which is used to compute cumulative exposure) is a function of a) the number of samples used to compute the mean, b) the between-sample variability, and c) the nature of the underlying distribution. However, the authors do not provide information on the number of samples collected, or on the degree of between-sample variability. Therefore, in the absence of data, the default assumption described in Appendix C is applied to this study to account for measurement error, and is characterized as:

PDF(measurement error) ~ TRI(0.6, 1, 1.5)

Uncertainty in Mean Values for Exposure Groups

The authors report cumulative exposures as ranges and as means for the six exposure groups. Since the mean values were reported by the authors, there is no reason to specify an uncertainty distribution for assuming the average of a reported range as the true mean.

Uncertainty in Conversion Factor (CF) from Dust Data (mppcf) to PCM f/cc

Peto et al. (1985) reported data on the relationship between paired dust measurements collected using the Casella thermal precipitator method and fiber concentrations measurements obtained using the Ottway long-running thermal precipitator method at an asbestos product plant in Rochdale, England. The data were from 18 different locations in the plant and were collected in 1960 and 1961. The authors used the average of the ratios (35.3 particles per fiber) as the most robust estimate of CF. The authors did not report on the uncertainty around this average ratio, but did present the data in graphical format (see Figure C.1 in the report by Peto et al. 1985). Based on this figure, the standard deviation in the ratios is estimated to be about 15, corresponding to a standard error of the mean (based on 18 observations) of about 3.5, which equates to a CV of about 0.1. Thus, uncertainty in the site-specific conversion factor at this plant may be modeled as:

PDF(conversion factor) ~ NORMAL(1, 0.1)

Uncertainty in the Use of Stationary Rather Than Personal Air Monitors

Stationary monitors were used to collect environmental measurements at the Rochdale factory. As discussed in Appendix C, use of stationary monitors may tend to underestimate the true exposure level of workers, especially those engaged in activities that actively disturb asbestos-containing materials or dusts. Based on available data on the ratio of particulate concentrations measured using personal to stationary monitors at various locations, the uncertainty attributable to this source may be characterized as:

PDF(personal vs. stationary) ~ BETA(2 , 20, 0.9, 10)

Uncertainty in Temporal Representativeness

Routine measurements of the workplace atmosphere are available for the Rochdale factory from 1951 onward. The principal cohort evaluated by Peto et al. (1985) included men first employed in 1933 or later. The data for the period 1951-1960 was used as a basis for assessing exposure levels between 1933 and 1950. As described in Appendix C, if site-specific data is available for some of the exposure period, and some data must be extrapolated for earlier periods, uncertainty in temporal representativeness is considered to be medium and is characterized as follows:

PDF(temporal representativeness) ~ TRI(0.8, 1, 1.2)

Bias Correction Factor in Data Reported as CE Rather Than CE10

Peto et al. (1985) imposed a lag of five years to allow for the delay between exposure to asbestos and any resulting increase in lung cancer mortality. Although this lag is different than that assumed in the lung cancer risk model (10 years), this difference is judged to be sufficiently minor than no added uncertainty distribution is added.

Uncertainty in Cumulative Exposure for Mesothelioma Analysis

Peto et al. (1985) report mesothelioma incidence as a bi-variate function of time since first exposure (T) and duration (D). The average value of cumulative exposure (C·Q) is estimated using the mid-points of the T and D bins to calculate Q, and the study-wide average concentration value (C). An uncertainty distribution to account for an approximation approach as discussed in Section 3.7 of Appendix C, is not needed for this study.

Uncertainty in Fraction Amphibole

As noted above, the Rochdale factory used chrysotile asbestos as the principal raw ingredient in the manufacturing of textile products. Peto et al. (1985) reported that crocidolite comprised approximately 2.6% of the total amount of asbestos purchased at the factory. Because the amount purchased each year tended to vary, and because the estimate is based on mass rather than fiber counts, uncertainty around this point estimate is judged to be moderate, and is characterized as follows:

PDF(f_{amph}) ~ TRI(0.02, 0.026, 0.032)

Uncertainty in Particle Size Data for Chrysotile

As mentioned above, this plant used primarily chrysotile asbestos. Of the TEM data sets available (see Appendix B), 11 are based on chrysotile asbestos, and 3 of these data sets correspond to the textile industry. These data sets differ by operation as preparation, twisting, and weaving. These operations were all performed at the Rochdale plant, and there is no basis to select one TEM data set over the other. Therefore, the three chrysotile data sets based on the textile industry were combined. Since the assigned TEM data sets match on asbestos type and industry, the uncertainty in f_{size} for chrysotile is determined to be low, and is modeled as follows:

$$PDF(f_{size[chrysotile]}) \sim TRI(0.8, 1, 1.2)$$

Uncertainty in Particle Size Data for Amphibole

Both crocidolite and amosite asbestos were used in this factory, although amosite was only used experimentally and is assumed to be negligible in contributing to worker exposures. Of the TEM data sets available (see Appendix B), 18 are based on amphibole asbestos. Eight of these data sets are based on crocidolite asbestos. Of these eight, five are from the mining industry and three are from the cement manufacturing industry. Because none of the data sets match on industry (textiles), there is no basis to choose one crocidolite TEM data set over the other, so all eight TEM crocidolite data sets were combined and applied to this study. As described in Appendix C, if TEM data sets are available that match on mineral form but not on industry, the uncertainty in f_{size} for amphibole is determined to be medium, and is modeled as follows:

$$PDF(f_{size[amphibole]}) \sim TRI(0.5, 1.0, 1.5)$$

Figure A9-1. Lung Cancer Data for British Textile Workers

CE_{10} (mppcf-yr)		CE_{10} (PCM f/cc-yr)	Observed	Expected	Relative Risk		
Range (a)	Mean (a)	Mean (b)	Deaths (a)	Deaths (a)	Pt. Est.	5% LB	95% UB
<1000	209	5.9	34	29.5	1.2	0.9	1.5
1000-2000	1409	39.9	8	7.7	1.0	0.6	1.8
2000-3000	2511	71.1	11	6.6	1.7	1.0	2.7
3000-4000	3474	98.4	6	5.7	1.1	0.5	2.0
4000-5000	4551	128.9	10	4.3	2.3	1.4	3.8
>=5000	9057	256.6	24	10.8	2.2	1.6	3.1

a) Data reported in Table 16 (Peto et al. 1985).

b) The authors report a conversion factor of 35.3 particles per fiber based on paired measurements.

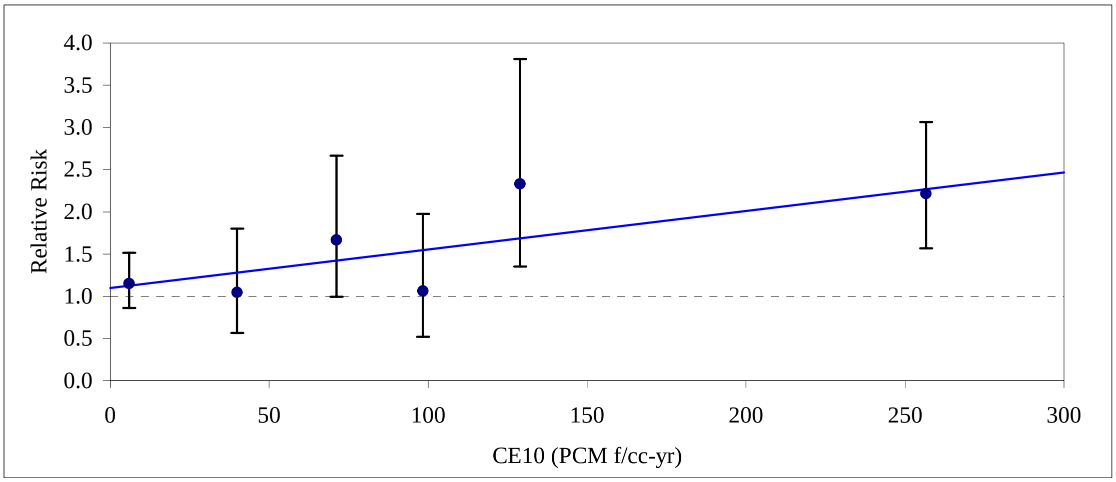
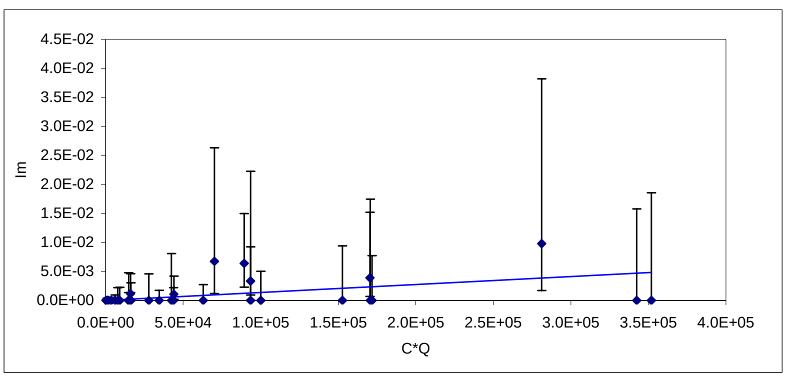


Figure A9-2. Mesothelioma Data for British Textile Workers

	Yrs since start			Duration								Incidence	Uncertainty Bounds	
Group	Min (a)	Max (a)	Midpoint	Min (a)	Max (a)	Midpoint	Q	C (b)	C*Q	Cases (a)	PY (a)	(Im)	5% LB	95% UB
1	10	20	15	0	1	0.5	33.9	8.21	278	0	28015	0.0E+00	7.0E-08	6.9E-05
2	10	20	15	1	4	2.5	109.4	8.21	898	0	4785.6	0.0E+00	4.1E-07	4.0E-04
3	10	20	15	5	9	7	125.0	8.21	1026	0	8520.5	0.0E+00	2.3E-07	2.3E-04
4	10	20	15	10	19	15	125.0	8.21	1026	0	4814.1	0.0E+00	4.1E-07	4.0E-04
5														
6														
7	20	25	22.5	0	1	0.5	225.1	8.21	1848	0	4668.2	0.0E+00	4.2E-07	4.1E-04
8	20	25	22.5	1	4	2.5	953.1	8.21	7824	0	877.4	0.0E+00	2.2E-06	2.2E-03
9	20	25	22.5	5	9	7	1786.8	8.21	14668	0	1416.8	0.0E+00	1.4E-06	1.4E-03
10	20	25	22.5	10	19	15	1953.1	8.21	16033	0	1423.3	0.0E+00	1.4E-06	1.3E-03
11	20	25	22.5	20	29	25	1953.1	8.21	16033	1	848.3	1.2E-03	2.1E-04	4.6E-03
12														
13	25	30	27.5	0	1	0.5	446.4	8.21	3664	0	3469.8	0.0E+00	5.7E-07	5.5E-04
14	25	30	27.5	1	4	2.5	1984.4	8.21	16290	0	631.7	0.0E+00	3.1E-06	3.0E-03
15	25	30	27.5	5	9	7	4201.8	8.21	34493	0	1103.5	0.0E+00	1.8E-06	1.7E-03
16	25	30	27.5	10	19	15	5332.4	8.21	43774	0	869.7	0.0E+00	2.3E-06	2.2E-03
17	25	30	27.5	20	29	25	5359.4	8.21	43996	1	935.3	1.1E-03	1.9E-04	4.2E-03
18														
19	30	35	32.5	0	1	0.5	742.6	8.21	6096	0	2041.2	0.0E+00	9.6E-07	9.4E-04
20	30	35	32.5	1	4	2.5	3390.6	8.21	27834	0	421.3	0.0E+00	4.7E-06	4.6E-03
21	30	35	32.5	5	9	7	7666.8	8.21	62937	0	707.2	0.0E+00	2.8E-06	2.7E-03
22	30	35	32.5	10	19	15	10878.6	8.21	89304	3	469.7	6.4E-03	2.3E-03	1.5E-02
23	30	35	32.5	20	29	25	11390.6	8.21	93507	2	599.7	3.3E-03	9.6E-04	9.2E-03
24	30	35	32.5	30	40	35	11390.6	8.21	93507	0	86.2	0.0E+00	2.3E-05	2.2E-02
25	35	40	37.5	0	1	0.5	1113.9	8.21	9144	0	840.4	0.0E+00	2.3E-06	2.3E-03
26	35	40	37.5	1	4	2.5	5171.9	8.21	42456	0	237.7	0.0E+00	8.3E-06	8.1E-03
27	35	40	37.5	5	9	7	12181.8	8.21	100001	0	383.3	0.0E+00	5.1E-06	5.0E-03
28	35	40	37.5	10	19	15	18599.9	8.21	152688	0	204	0.0E+00	9.6E-06	9.4E-03
29	35	40	37.5	20	29	25	20769.9	8.21	170502	1	257.1	3.9E-03	6.8E-04	1.5E-02
30	35	40	37.5	30	40	35	20796.9	8.21	170723	0	109.9	0.0E+00	1.8E-05	1.7E-02
31	40	50	45	0	1	0.5	1811.4	8.21	14870	0	402.3	0.0E+00	4.9E-06	4.8E-03
32	40	50	45	1	4	2.5	8546.9	8.21	70162	1	148.4	6.7E-03	1.2E-03	2.6E-02
33	40	50	45	5	9	7	20923.0	8.21	171759	0	249.1	0.0E+00	7.9E-06	7.7E-03
34	40	50	45	10	19	15	34259.9	8.21	281242	1	102.3	9.8E-03	1.7E-03	3.8E-02
35	40	50	45	20	29	25	41717.4	8.21	342462	0	121.7	0.0E+00	1.6E-05	1.6E-02
36	40	50	45	30	40	35	42875.0	8.21	351965	0	103.4	0.0E+00	1.9E-05	1.9E-02

(a) Reported in Table 8 (Peto et al. 1985)
(b) Calculated as average from data on mean dust levels (f/cc) 1936-1972 provided in Table 6 (Peto et al. 1977).



A10. Italian Chrysotile Mine

References

Primary: Piolatto, G., Negri, E., La Veccia, C., Pira, E., Decarli, A., and Peto, J. (1990). An update of cancer mortality among chrysotile asbestos miners in Balangero, Northern Italy. *British Journal of Industrial Medicine*, **47**, 810-814.

Other: Rubino, G., Piolatto, F., Newhouse, M., Scansetti, G., Aresini, G., and Murray, (1979). Mortality of chrysotile asbestos workers at the Balangero Mine, Northern Italy. *British Journal of Industrial Medicine*, **36**, 187-194.

Ghezzi, I, Aresini, G., and Vigliani, E. (1972). Il rischio di asbestosi in una miniera di amianto crisotilo. *La Medicina del Lavoro*, **5-6**, 33-56.

Study Description

Location and Facility Description

The mine is located in Balangero, Italy, which is located in the foothills of the Alps (near Turin, northern Italy). The mine, an open pit type, and its associated milling, crushing, screening and bagging plant began production of chrysotile asbestos in 1916 and, with the exception of the war years from 1939 to 1945, production has increased each year. By 1990, the mine was producing 500 tons of asbestos per day from the crushing of 9,000 tons of serpentine rock.

Asbestos Type

The mine produces chrysotile asbestos. An examination of several air samples using SEM did not find amphibole fibers at detectable concentrations. The analytical sensitivity of the analysis was not reported, so trace levels of amphibole could have been present but undetected. A fibrous silicate known as balangeroite accounts for 0.2% - 0.5% of the total mass of commercial product from the mine. The smallest diameters of balangeroite were found to be on the same order as amphibole asbestos (around 0.1 – 2.0 um). The adverse effects associated with balangeroite exposure are not well characterized, but the authors theorized that, based on fiber dimensions and mineral properties, balangeroite might produce effects in humans similar to those of amphibole asbestos.

Fraction Amphibole

Although Piolatto et al. (1990) reported that SEM results revealed no detectable amphibole fibers, their analysis was based on a small number of samples and no details of their analytical sensitivities were reported. As discussed in Appendix C, chrysotile is often contaminated with trace levels of tremolite amphibole. Therefore, it is considered possible that trace levels of amphibole could have been present but undetected. On this basis, as discussed in Appendix C, the estimated average level of amphibole for the Italian mine is assumed to be about 0.054%.

Cohort Description and Follow-up

The cohort was comprised of men who had worked for at least one year at the factory between 1946 and 1987. Based on this definition, a total of 1,094 workers were identified for inclusion in this cohort. Follow-up was carried out from January 1, 1946 through December 31, 1987. Thirty-six men (3%) were excluded because their vital status could not be ascertained. Thus, the total cohort included 1,058 men.

Determination of Cause of Death and Diagnosis of Lung Cancer/Mesothelioma Cases

A total of 427 deaths were registered for this cohort that encompassed a total of 27,010 man-years of observation. Causes and dates of death for members of the cohort were obtained through population registries and copies of death certificates obtained from municipal registration offices. Rubino et al. (1979) noted that the cause of death on death certificates were in accord with the seventh revision of the International Classification of Diseases (ICD). Diagnoses of mesothelioma deaths were based on clinical and radiological findings. For the two pleural mesothelioma deaths reported, one was confirmed by examination of pleural fluid and the other was confirmed by histological examination of specimens from a thoracotomy.

Reference Population

Expected deaths were computed using Italian national death rates for each five year calendar period and age group. National numbers are published by the Central Institute of Statistics from 1955 forward. Rates for the late 1950's were used for the period 1946-1954. The authors note the SMRs for alcohol-related diseases may be overestimated slightly by using national mortality rates instead of local mortality rates to calculate expected deaths. In the case of laryngeal cancer, the authors noted that excess mortality was evident in the general population around Balangero.

Estimating Exposure Concentration

Beginning in 1969, measurements of asbestos levels in workplace air were made using the membrane filter method. In order to estimate asbestos levels that existed before 1969, factory archives and long-time workers were consulted in order to characterize previous exposure conditions. An area of the plant was then used to simulate the previous conditions, and samples of air were collected on filters and analyzed by PCM.

Estimating Cumulative Exposure

Cumulative exposures for the Italian miners were characterized according to information obtained from personnel records including dates of birth and employment and job category. Rubino et al. (1979) attempted to quantify each individual's exposure as most workers changed jobs during their working life at the mine. The cumulative exposure (PCM f/cc-yrs) for each worker in each year of employment was calculated by summing the concentration values for each year in each employment category. Employment dates were lagged by one year in calculating exposure estimates to account for retirement or change of job due to the disease itself. The authors noted that changing this to two or three years did not have a significant effect. A mean value across all jobs was applied to workers with missing job descriptions (N=38), and to maintenance workers. For comparison of earlier re-created conditions to current conditions, weighting factors based on available information regarding work durations (e.g. only worked 1 to 2 hours per day in many of the dustier operations like drilling) were applied to the simulated concentrations. Further detail of these weighting factors is not provided.

Smoking Data

Piolatto et al. (1990) did not provide data on the smoking status of the workers in this cohort. However, in an earlier study on this cohort, Rubino et al. (1979) reported that all 11 cases of lung cancer observed at that time occurred in smokers. The authors stated that the data were not sufficient to examine whether the additive or multiplicative model for asbestos and cigarette smoking and lung cancer was applicable.

Lung Cancer Results

Person-years of observation for each worker were stratified into three exposure groups based on cumulative exposure (PCM s/cc-yrs), and relative risk was computed based on a comparison of observed and expected numbers of lung cancer deaths. ICD code not reported, but as laryngeal cancer and pleural cancer were reported separately it is assumed to be ICD

162 which includes cancer of the trachea, bronchus, and lung. The raw data (taken from Table 3 of Piolatto et al. 1990) are summarized in Figure A10-1. The relative risk of lung cancer was not statistically different from 1.0 for any exposure group, although the MLE linear regression line through the data did have a positive slope.

Mesothelioma Results

Two mesothelioma deaths were observed in the cohort. Both cases were in workers whose first exposure had occurred at least 20 years earlier. The authors stated that the expected value for mesothelioma was 0.3, but did not describe how they derived this value.
In order to apply the OSWER mesothelioma model, it is necessary to estimate the duration of exposure and level of exposure for each category. Based on the data presented in Table 3 of Piolatto et al. (1990), the population-weighted average time since first exposure and time since last exposure can be calculated. From these, the population-weighted exposure duration is estimated as the difference of 5.94 years. Using this duration estimate and the data presented in Table 3 of Piolatto et al. (1990) by cumulative exposure, the population-weighted average exposure concentration can be estimated as 18.73 f/ml. The resulting estimates of cumulative exposure (C·Q) are shown in Figure A10-2.

Uncertainty and Bias Characterization

Appendix C discusses the primary sources of uncertainty in epidemiological studies of cancer risk from asbestos exposure in the workplace and describes the methods used in this document for characterizing the uncertainty. The following sections discuss the uncertainty characterization and issues of potential bias for this study.

Uncertainty Due to Measurement Error

As described in Section 3.1 of Appendix C, all estimates of concentration levels of asbestos in the workplace are uncertain due to the combination of sampling error and analytical error. These measurements are usually averaged according to job or work area, often stratified by time. For this study, Rubino et al. (1979) report mean concentrations as a function of time period and operation (see Table 1 in the original report). The magnitude of the uncertainty in the reported mean value for each job/time category (which is used to compute cumulative exposure) is a function of a) the number of samples used to compute the mean, b) the between-sample variability, and c) the nature of the underlying distribution. However, the authors do not provide information on the number of samples collected, or on the degree of between-sample variability. Therefore, in the absence of data, the default assumption described in Appendix C is applied to this study to account for measurement error, and is characterized as:

PDF(measurement error) ~ TRI(0.6, 1, 1.5)

Uncertainty in Mean Values for Exposure Groups

The authors report cumulative exposure values as ranges for the three exposure groups. For the two exposure groups with bounded ranges, the mid-point of the range is taken as the point estimate. As discussed in Appendix C, this point estimate is an uncertain estimate of the true mean, and the uncertainty is characterized as follows:

PDF(exposure, bounded) ~ TRI(Min/Mid, 1, Max/Mid)

For the highest exposure group with an unbounded range (CE ≥ 400 f/cc-yr), the point estimate and uncertainty is modeled as:

PDF(exposure, unbounded) ~ TRI(1, 5/3, 3)

Uncertainty in Conversion Factor (CF) from Dust Data (mppcf) to PCM f/cc

In this study, workplace air measurements were available from 1969 onward. Although details were not provided, these measurements were of "fiber counts" as reported by Rubino et al. (1979), so it is assumed the data were based on the filter method using PCM-based counting rules. Thus, no uncertainty factor is needed to account for extrapolation from dust to fibers concentrations.

Uncertainty in the Use of Stationary Rather Than Personal Air Monitors

No details were provided on whether the air measurements were collected using stationary or personal air monitors. In the absence of knowledge, it is assumed the measures were collected using stationary monitors. As discussed in Appendix C, use of stationary monitors may tend to underestimate the true exposure level of workers, especially those engaged in activities that actively disturb asbestos-containing materials or dusts. Based on available data on the ratio of particulate concentrations measured using personal to stationary monitors at various locations, the uncertainty attributable to this source may be characterized as:

PDF(personal vs. stationary) ~ BETA(2, 20, 0.9, 10)

Uncertainty in Temporal Representativeness

The cohort is defined as employees who had worked for at least one year between 1946 and 1987. As noted above, air measurements were collected at the mine beginning in 1969. For periods before 1969, Rubino et al. (1979) recreated conditions in the plant comparable to those occurring at various periods between 1946 and 1975. Measurements for the period prior to 1946 were made under simulated conditions based on anecdotal information from former employees and information in factory archives. Rubino et al. (1979) specifically noted that estimated values for past fiber concentrations have considerable limitations that do not account for individual variation among workers or variations due to external sources such as weather (e.g. ventilation differences due to open windows or air conditioning on hot days versus cold days) which could have a significant effect in the amount of dust in the air.

As discussed in Appendix C, when data must be predominantly extrapolated the uncertainty used to characterize temporal representativeness is ranked as high. However, since the authors actually simulated conditions that workers were exposed to, uncertainty is considered to be medium and is characterized as follows:

PDF(temporal representativeness) ~ TRI(0.8, 1, 1.2)

Bias Correction Factor for Data Reported as CE Rather Than CE10

As discussed in Appendix C, use of CE rather than CE10 tends to bias results low, with the magnitude depending on the duration of exposure, the length of follow-up, and whether or not early person years of observation were excluded. Piolatto et al. (1990) does not report the average duration, but based on available information, an average duration of 10 years was estimated. Follow-up ended in 1987, and the average time since last exposure was estimated based on this information to be 26 years. Piolatto et al. (1990) did not mention the restriction of a latency period on the mortality data for the Italian miners. Based on this information, a BCF was estimated as described in Appendix C with the following parameters:

BCF ~ TRI(1.5, 1.6, 1.7)

Uncertainty in Cumulative Exposure for Mesothelioma Analysis

This study reports mesothelioma incidence as a mono-variate function of time since first exposure (T). The average value of cumulative exposure ($C \cdot Q$) is estimated from the mid-point of the T bins (reported in Table 3 of Piolatto et al. 1990). Average duration of the cohort was not reported, neither was average concentration of asbestos fibers in air for the factory. However, these values can be estimated as person-year weighted averages from the data reported in Table 3 as described above. As discussed in Section 3.7 of Appendix C, this

approximation approach introduces uncertainty into the study-specific dose-response relationship, and this uncertainty may be approximated as follows:

$$PDF(\text{approximation of } C \cdot Q) \sim TRI\ (0.75, 1, 1.4)$$

Uncertainty in Fraction Amphibole

As noted above, the Italian mine is characterized as a chrysotile mine with no known amphibole asbestos. However, as described in Appendix C, chrysotile asbestos is often contaminated with trace levels of tremolite amphibole. Therefore, the uncertainty distribution around the point estimate of 0.054% is characterized as:

$$PDF(f_{amph}) \sim LN(0.00054, 0.001)$$

Uncertainty in Particle Size Data for Chrysotile

As mentioned above, the Italian mine evaluated by this study was a chrysotile mine. Of the TEM data sets available (see Appendix B), 11 are based on chrysotile asbestos. Two of these data sets correspond to the mining/milling industry. These data sets which differ by operation as mining and bagging were combined. Since the assigned TEM data sets match on asbestos type and industry, the uncertainty in f_{size} for chrysotile is determined to be low, and is modeled as follows:

$$PDF(f_{size[chrysotile]}) \sim TRI(0.8, 1, 1.2)$$

Uncertainty in Particle Size Data for Amphibole

The Italian miners were reported to have only been exposed to chrysotile asbestos. However, as described in Appendix C and detailed in Addison and Davies (1990), tremolite may occur as a contaminant in chrysotile asbestos. There is only one TEM data set for tremolite asbestos and it is based on the mining/milling industry. In accord with the general approach described in Appendix C, when the TEM data set matches on amphibole type and industry, uncertainty is ranked as low and is characterized by:

$$PDF(f_{size[amphibole]}) \sim TRI(0.8, 1, 1.2)$$

Figure A10-1. Raw Lung Cancer Data for the Italian Chrysotile Mine

CE (PCM f/cc-yr)		Observed Deaths (a)	Expected Deaths (a)	RR		
Range (a)	Mean (b)			Point Est	5% LB	95% UB
< 100	50	4	5.1	0.8	0.3	1.7
100 - 400	250	8	6.1	1.3	0.7	2.3
> 400	666.7	10	8.7	1.1	0.7	1.9

a) Data reported in Table 3 (Piolatto et al. 1990).

b) Calculated as the midpoint of the reported range of CE, except for the highest exposure group which has an unbounded range. The point estimate is assigned a value = 5/3*lower bound.

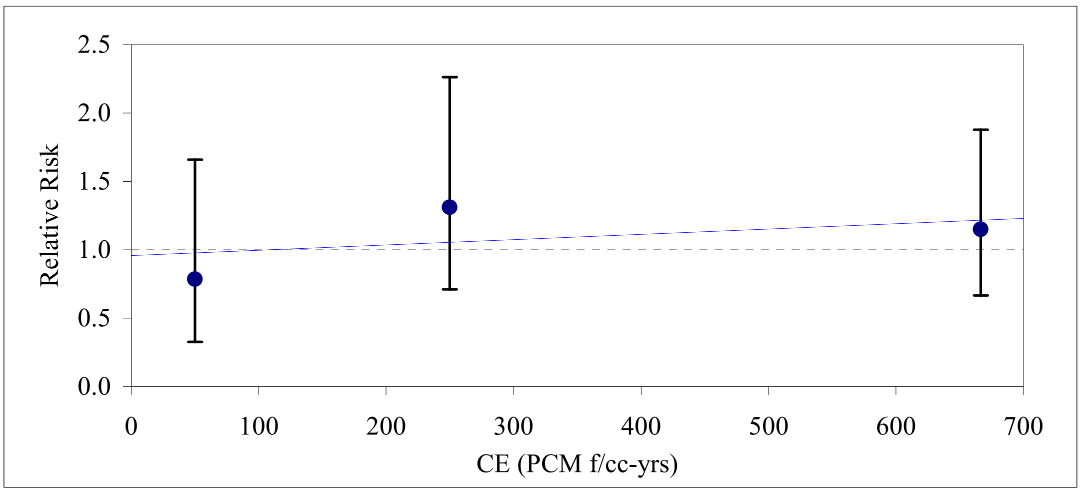


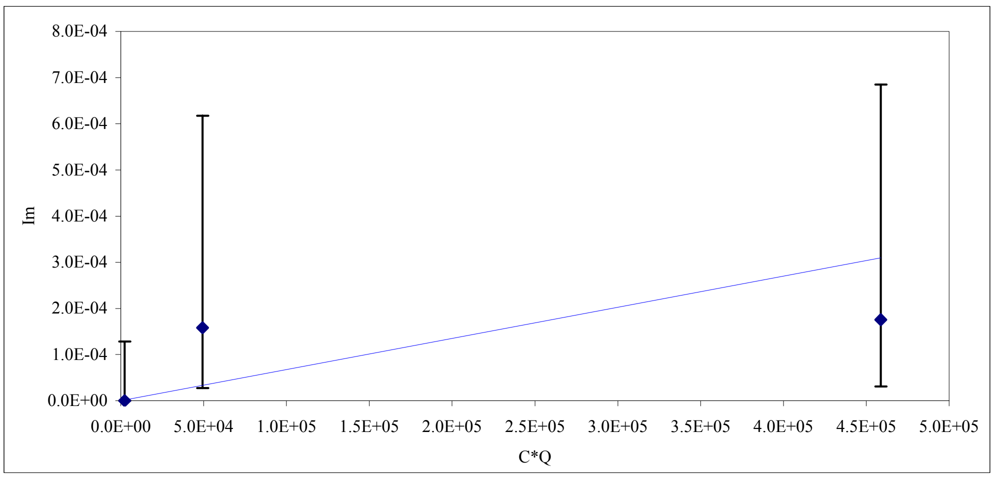
Figure A10-2. Raw Mesothelioma Data for the Italian Chrysotile Mine

Yrs Since Start		Exp. Duration	Exposure	Q	PY (a)	Observed	Incidence	Uncertainty Bounds	
Range (a)	Midpoint	(b)	Conc (c)			Deaths (a)	(Im)	5% LB	95% UB
<20	15	5.94	18.73	125.00	14983	0	0.00E+00	1.3E-07	1.3E-04
20-30	25	5.94	18.73	2632.04	6325	1	1.58E-04	2.8E-05	6.2E-04
>30	50	5.94	18.73	24497.72	5702	1	1.75E-04	3.1E-05	6.9E-04

(a) Reported in Table 3 (Piolatto et al. 1990)

(b) Calculated value based on data reported in Table 3 (Piolatto et al. 1990). Estimated based on the difference between the person-year weighted average time since first exposure and the person-year weighted average time since last exposure.

(c) Calculated value. Estimated based on dividing the person-year weighted average cumulative exposure from data presented in Table 3 (Piolatto et al. 1990) by the estimated duration value of 5.94 years.



A11. New Jersey Pipe Insulation Manufacturing Plant

References

Primary: Seidman, H., Selikoff, I. J., and Gelb, S. K. (1986). Mortality experience of amosite asbestos factory workers: dose-response relationships 5 to 40 years after onset of short-term work exposure. *American Journal of Industrial Medicine* **10**:479-514.

Other: Seidman, H., Selikoff, I. J., and Hammond, E. C. (1979). Short-term asbestos work exposure and long-term observation. *Annals of the New York Academy of Sciences* **330**:61-89.

Study Description

Location and Facility Description

The factory is located in Patterson, New Jersey. The factory was established to supply asbestos insulation to the U.S. Navy for pipes, boilers, and turbines of its ships for World War II. Operations began in June 1941 and continued through November 1954.

Asbestos Type

Amosite asbestos was used almost exclusively at this factory. The amosite was obtained from Africa as crushed stone and was broken down by pulverizers at the factory. No crocidolite and "very little" chrysotile were used.

Fraction Amphibole

The meaning of "very little" chrysotile is not discussed in the report. Assuming that this implies that < 1% chrysotile was used in products, the point estimate selected for the fraction amphibole in the workplace atmosphere is 99%.

Cohort Description and Follow-up

The cohort consisted of 933 men (mostly white) who began work in the plant between June 1941 and December 1945. Of these, 113 were excluded from the study because they had prior asbestos exposure (21 men), or because they either a) took up asbestos work elsewhere (14 men), b) died (40 men), or c) were lost to follow-up (38 men) before attaining a latency of five years after first employment in the plant. This left a set of 820 men (18,190 person-years) with a minimum of 5 years of observation who were retained for evaluation.

Turnover in the New Jersey workforce was high, especially during war years when men were being drafted in to the armed services. This resulted in men starting work at the factory at an older age, as young men were not as available during wartime. Over 60% of the workforce was only employed for less than one year, and 23% of the workforce was employed for two years or longer.

Follow-up was performed as of December 31, 1982. At that time, five additional men were lost to follow-up. Six men who took up asbestos-related work in another location after 5 years were retained, but only through the time that the other exposure began. By the end of follow-up, 593 men (72%) were dead.

The authors noted that this cohort is unique in that a large proportion of this group had high but brief exposures to amosite in the plant, followed by long observation.

Determination of Cause of Death and Diagnosis of Lung Cancer/Mesothelioma Cases

Cause of death was obtained from death certificates coded by the sixth, seventh, and eighth revisions of the International Classification of Diseases (ICD). The observed deaths were coded both according to the death certificate information, and also according to the "best evidence" established from additional information from autopsy, surgical specimens, x-ray films, and clinical findings.

Reference Population

Expected mortality was calculated from age- and year-specific rates for New Jersey white males.

Estimating Exposure Concentration

No measures of asbestos in workplace air are available for this plant. The authors stated that it was obvious the plant was quite dusty, with certain areas and jobs (e.g., pulverizer, dumping bags, feeding hoppers, filling bins) being much dustier than others. In the absence of plant-specific data, estimates of workplace exposure levels were based on measurements available from studies by NIOSH between 1967 and 1971 at two similar plants located in Tyler, Texas, and Port Allegheny, Pennsylvania. These two plants were operated by the same company, made the same products, and used some of the same machinery as the Patterson facility. Based on these data, the estimated levels of asbestos in the Patterson plant, stratified according to 31 different jobs or areas, ranged from 5 to 120 PCM f/cc. Based on these data (see Table XIII in Seidman et al. 1986), the population-weighted average concentration was 47 PCM f/cc and the median was 50 PCM f/cc.

Estimating Cumulative Exposure

The authors utilized job histories for each worker to identify the number of years worked in each job or area of the plant. Cumulative exposure for each worker was estimated as the sum of concentration multiplied by the exposure duration in each job/location.

Smoking Data

No data on the smoking patterns of workers in this cohort were reported.

Lung Cancer Results

Data on the occurrence of lung cancer as a function of cumulative exposure are presented in Table XVI of Seidman et al. (1986). These data are shown in Figure A11-1. As seen, a clear exposure-response relationship is apparent.

Mesothelioma Results

Based on the "best evidence" approach, Seidman et al. (1986) identified 17 deaths from mesothelioma in this population. Table III of Seidman et al. (1986) categorized mesothelioma deaths and person-years of observation by years since onset of work. In order to apply the OSWER mesothelioma model, it is necessary to estimate the duration of exposure and level of exposure for each category. Based on the data presented in Table IV of Seidman et al. (1986), the population-weighted average exposure duration is 0.94 years. Based on the data in Table XIII of Seidman et al. (1986), the population-weighted average exposure level is 47 f/cc. The resulting estimates of cumulative exposure (C·Q) are shown in Figure A11-2.

Bias, Confounding, and Misclassification Issues

Because no measures of asbestos concentration in air were performed in this plant, estimates of exposure are particularly uncertain, with the potential for exposure misclassification. In addition, because no data were obtained on smoking prevalence, there could be differences between the cohort and the reference population that could influence relative risk estimates.

Uncertainty and Bias Characterization

Appendix C discusses the primary sources of uncertainty in epidemiological studies of cancer risk from asbestos exposure in the workplace and describes the methods used in this document for characterizing the uncertainty. The following sections discuss the uncertainty characterization and issues of potential bias for this study.

Uncertainty Due to Measurement Error

As described in Section 3.1 of Appendix C, all estimates of concentration levels of asbestos in the workplace are uncertain due to the combination of sampling error and analytical error. These measurements are usually averaged according to job or work area, often stratified by time. For this study, Seidman et al. (1986) report mean concentrations (for fibers greater than 5 um in length) by job (see Table XIII in the original report). The magnitude of the uncertainty in the reported mean value for each job/time category (which is used to compute cumulative exposure) is a function of a) the number of samples used to compute the mean, b) the between-sample variability, and c) the nature of the underlying distribution. However, the authors do not provide information on the number of samples collected, or on the degree of between-sample variability. Therefore, in the absence of data, the default assumption described in Appendix C is applied to this study to account for measurement error, and is characterized as:

PDF(measurement error) ~ TRI(0.6, 1, 1.5)

Uncertainty in Mean Values for Exposure Groups

The authors report cumulative exposure values as ranges for eight exposure groups. For the first seven groups with bounded ranges, the mid-point of the range is taken as the point estimate. As discussed in Appendix C, this point estimate is an uncertain estimate of the true mean, and the uncertainty is characterized as follows:

PDF(exposure, bounded) ~ TRI(Min/Mid, 1, Max/Mid)

The highest exposure group is unbounded (> 250 f/cc). As discussed in Appendix C, in this case the point estimate and uncertainty is modeled as:

PDF(exposure, unbounded) ~ TRI(1, 5/3, 3)

Uncertainty in Conversion Factor (CF) from Dust Data (mppcf) to PCM f/cc

Workplace air measurements applied to this cohort were collected by the U.S. Public Health Service in 1967, 1970 and 1971 at plants in Texas and Pennsylvania as described above. Although details were not provided, these measurements were of “fiber counts”, so it is assumed the data were based on the filter method using PCM-based counting rules. Thus, no uncertainty factor is needed to account for extrapolation from dust to fibers concentrations.

Uncertainty in the Use of Stationary Rather Than Personal Air Monitors

No details were provided on whether the air measurements collected by the U.S. Public Health Service utilized stationary or personal air monitors. In the absence of knowledge, it is assumed the measures were collected using stationary monitors. As discussed in Appendix C, use of stationary monitors may tend to underestimate the true exposure level of workers, especially those engaged in activities that actively disturb asbestos-containing materials or dusts. Based on available data on the ratio of particulate concentrations measured using personal to stationary monitors at various locations, the uncertainty attributable to this source may be characterized as:

PDF(personal vs. stationary) ~ BETA(2, 20, 0.9, 10)

Uncertainty in Temporal Representativeness

As noted above, the data used to estimate concentration values in the Patterson plant, which operated from 1941 to 1954, were collected in two other plants in the 1967-1971 time frame. Seidman et al. (1979) stated that “dust extraction equipment was likely to have been better in the latter period of time”, implying that measurements made in 1967-71 were likely lower than would have existed during the earlier time the plant was operating. It is assumed that this information was accounted for when data from the Tyler and Port Allegheny plants were extrapolated to the Patterson plant, but nevertheless, this is an important source of uncertainty. As discussed in Appendix C, when data are considered to be poorly representative over time, uncertainty is considered to be high and is characterized as follows:

PDF(temporal representativeness) ~ TRI(0.5, 1, 1.5)

Uncertainty Due to Extrapolation Across Plants

As noted above, data on workplace levels of asbestos were never collected in the Patterson plant. Rather, estimates of concentration were based on extrapolations from other plants engaged in the same operations. These plants were operated by the same company and followed the same production processes using amosite asbestos from the same source material. Some of the same machinery was used between plants as well. However, ventilation may have differed significantly. Seidman and Selikoff (1986) specifically noted that general conditions in the other plants may have been better than at the New Jersey plant. The magnitude and direction of any error introduced by the extrapolation of concentration data across plants is not known. In the absence of additional information, this source of uncertainty is addressed by application of the following extra uncertainty distribution:

PDF(spatial representativeness) ~ TRI(0.8, 1, 1.2)

Bias Correction Factor for Data Reported as CE Rather Than CE10

This study reported cumulative exposure as CE rather than as CE10. As discussed in Appendix C, use of CE rather than CE10 tends to bias results low, with the magnitude depending on the duration of exposure, the length of follow-up, and whether or not early person years of observation were excluded. Seidman and Selikoff (1986) do not report the average duration, but based on the data reported in table IV, the population-weighted average exposure duration is 0.94 years. Follow-up ended in 1982, and the average time since last exposure was estimated as 35 years. The mortality data presented by Seidman et al. (1986) are based on the exclusion of the first five years after onset of exposure. Based on these study attributes a BCF for this cohort was determined to be:

BCF ~ TRI(1.18, 1.21, 1.27)

Uncertainty in Cumulative Exposure for Mesothelioma Analysis

This study reports mesothelioma incidence as a mono-variate function of time since first exposure (T). The average value of cumulative exposure (C·Q) is estimated from the mid-point of the T bins (reported in Table 3 of Seidman et al. 1986) and estimates of the average exposure concentration and average exposure duration for the entire cohort, as described above. As discussed in Section 3.7 of Appendix C, this approximation approach introduces uncertainty into the study-specific dose-response relationship, and this uncertainty may be approximated as follows:

PDF(use of approximation method) ~ TRI (0.75, 1, 1.4)

Uncertainty in Fraction Amphibole

As noted above, this plant is characterized as having used primarily amosite with no crocidolite and “very little” chrysotile. In the absence of further information on what “very little” may imply, the uncertainty distribution for f_{amph} is taken to be:

$PDF(f_{amph}) \sim TRI(0.95, 0.99, 1.00)$

Uncertainty in Particle Size Data for Chrysotile

As mentioned above, the factory evaluated by this study used primarily amphibole asbestos and “very little” chrysotile. Of the TEM data sets available (see Appendix B), 11 are based on chrysotile asbestos. None of these data sets correspond to the insulation manufacturing industry. The 11 data sets correspond to multiple industries including mining/milling, textiles, friction products, and cement manufacturing. It is not obvious which industry would most closely resemble the industry of insulation manufacturing, so all of the available chrysotile data sets were combined and applied to this study. Since there were no TEM data sets that matched on industry, the uncertainty in f_{size} for chrysotile is determined to be medium for this cohort, and is modeled as follows:

$PDF(f_{size[chrysotile]}) \sim TRI(0.5, 1, 1.5)$

Uncertainty in Particle Size Data for Amphibole

For this study, the primary type of asbestos used at the insulation factory was amosite. Of the TEM data sets available (see Appendix B), 18 are based on amphibole asbestos. Three of these data sets are based on amosite asbestos for the industry of pipe insulation manufacturing. These three data sets differ based on operation (mixing, forming, and finishing), all of which were performed in the Patterson plant. Therefore, these three TEM data sets were combined and applied to this study. Since the TEM data sets matched on amphibole type and industry, the uncertainty in f_{size} for amphibole is determined to be low for this cohort, and uncertainty in f_{size} is modeled as follows:

$$PDF(f_{size[amphibole]}) \sim TRI(0.8, 1.0, 1.2)$$

Figure A11-1. Raw Lung Cancer Data for the New Jersey Insulation Manufacturing Plant

CE (PCM f/cc-yr)		Observed	Expected	Relative Risk		
Range (a)	Mean (b)	Deaths (a)	Deaths (a)	Pt. Est.	5% LB	95% UB
<6	3	15	5.3	2.8	1.8	4.2
6-11.9	9	12	2.9	4.2	2.5	6.5
12-24.9	18.5	15	3.4	4.4	2.8	6.6
25-49.9	37.5	13	2.8	4.7	2.9	7.2
50-99.9	75	17	2.4	7.1	4.7	10.5
100-149.9	125	9	1.5	6.0	3.4	10.1
150-249.9	200	15	1.3	11.4	7.3	17.0
250+	416.7	15	0.9	16.0	10.3	23.9

a) Data reported in Table XVI (Seidman et al. 1986).

b) Calculated as the midpoint of the reported range of CE, except for the highest exposure group which has an unbounded range. The point estimate is assigned a value = 5/3*lower bound.

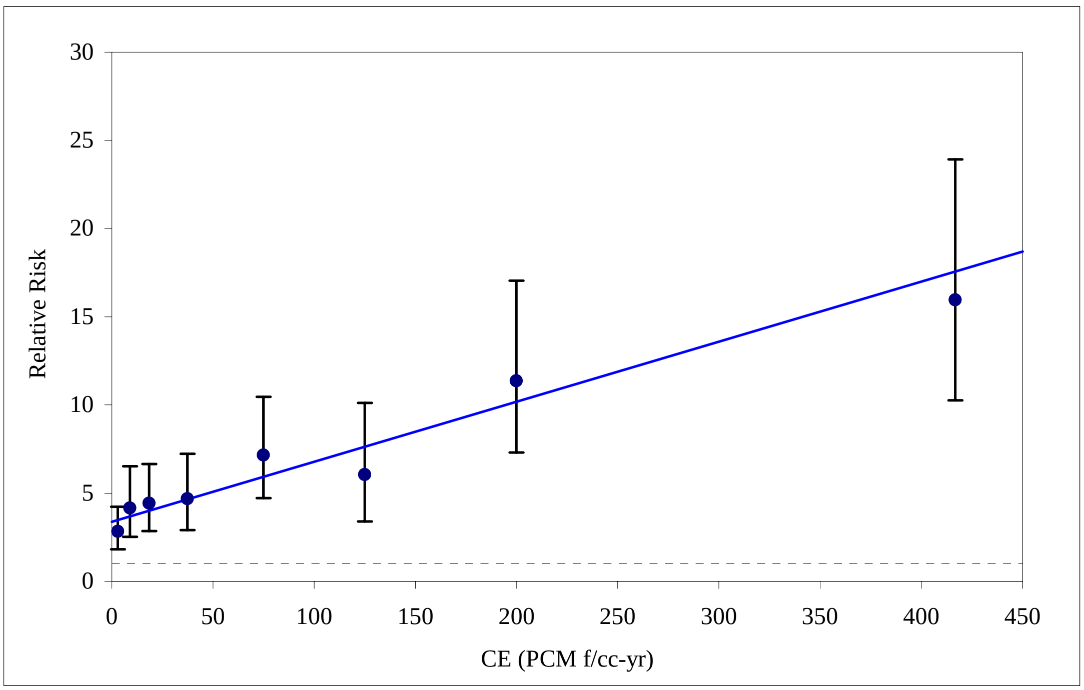
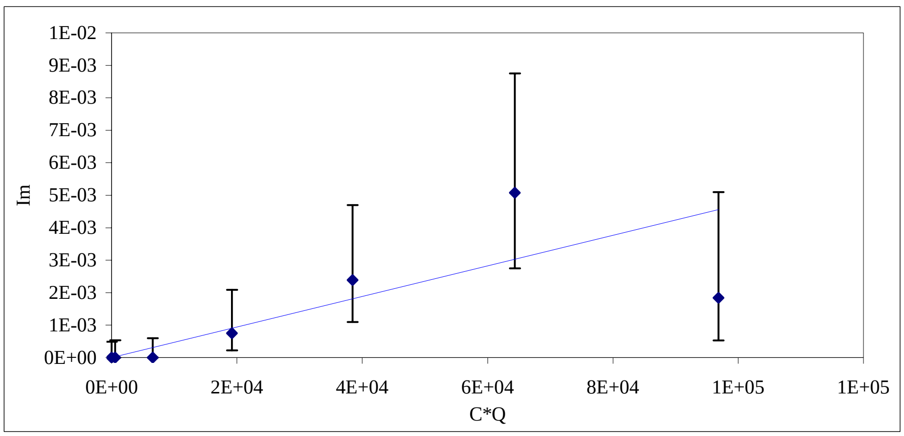


Figure A11-2. Raw Mesothelioma Data for the New Jersey Insulation Manufacturing Plant

Yrs Since 1st Employment		Exp. Duration	Exposure	Q	PY (a)	Observed	Incidence	Uncertainty Bounds	
Range (a)	Midpoint	(b)	Conc (c)			Deaths (a)	(Im)	5% LB	95% UB
5-9	7.5	0.94	47	0.0	3952	0	0.0E+00	5.0E-07	4.9E-04
10-14	12.5	0.94	47	11.8	3628	0	0.0E+00	5.4E-07	5.3E-04
15-19	17.5	0.94	47	139.6	3198	0	0.0E+00	6.1E-07	6.0E-04
20-24	22.5	0.94	47	408.3	2656	2	7.5E-04	2.2E-04	2.1E-03
25-29	27.5	0.94	47	818.1	2094	5	2.4E-03	1.1E-03	4.7E-03
30-34	32.5	0.94	47	1368.8	1576	8	5.1E-03	2.8E-03	8.8E-03
35-39	37.5	0.94	47	2060.6	1086	2	1.8E-03	5.3E-04	5.1E-03

(a) Reported in Table III (Seidman et al. 1986).
(b) Population weighted average exposure duration calculated from Table IV of Seidman et al (1986)
(c) Population-weighted average concentration based on data in Table XIII of Seidman et al. (1986)



A12. Swedish Cement Plant

References

Primary: Albin, M., Jakobsson, K., Attewell, R., Johansson, L., Welinder, H. (1990a). Mortality and cancer morbidity in cohorts of asbestos cement workers and referents. *British Journal of Industrial Medicine* 47:602-610.

Other: Albin, M., Johansson, L., Pooley FD, Jakobsson K, Attewell R, Mitha R. (1990b). Mineral fibers, fibrosis, and asbestos bodies in lung tissue from deceased asbestos cement workers. *British Journal of Industrial Medicine* 47:767-774.

Study Description

Location and Facility Description

The plant is located in a small community in southern Sweden. The plant began operation in 1907 and produced a variety of asbestos-containing cement products, including sheets, shingles, ventilation pipes, and various hand-molded details until 1978. The plant used Portland cement that had a low content (<0.1%) of crystalline silica in the respirable size range. All asbestos used at the plant was milled before mixing. Over the history of the plant, changes in machinery were made including changing from dry to wet milling in 1952, which allowed for use of shorter fibers. Starting in the later part of the 1960s, systematic efforts were made to reduce dust concentrations at the plant.

Asbestos Type

Mainly chrysotile (>95%) asbestos was used at this plant. Crocidolite was used before 1966, but never exceeded 3–4% of the total asbestos use at the factory. From 1953 through 1966, the amount of crocidolite used amounted to less than 1% of the total asbestos used. Amosite was used for a few years in the 1950s, but never exceeded 18% of the total asbestos used.

Fraction Amphibole

The data above suggest that the amount of amphibole in the workplace atmosphere may have varied somewhat over time, as follows:

From 1907 – 1953 (no bound on earliest year reported) :	< 1% crocidolite
From 1953 – 1966 :	< 3-4% crocidolite
From 1952 – 1955 (reported as a "few" years) :	< 18 % amosite

The time-weighted average based on these values is < 2.5%, so a point estimate of 2% is selected for use in this document.

Cohort Description and Follow-up

The total number of employees at the Swedish plant at one time reached a maximum of 450 employees in the mid-1960s. Turnover of the workforce was generally low. The cohort consisted of all male employees who worked for at least 3 months between 1907 and the end 1977. A total of 2,898 men met this definition. The total number of person-years was not reported.

Follow-up was carried out through December 31, 1986. Twenty percent of the cohort was lost to follow-up and were excluded from the analysis. Most of those workers lost to follow-up were immigrant workers. Immigrant workers were excluded from the analysis as they constituted 33% of the exposed cohort, compared to only 11% of the reference cohort (see description below). This reduced the size of the exposed cohort to 1,929 Swedish men. The total number of men within the cohort that had died by the end of follow-up was not reported. However, when restricting mortality based on a minimum latency period of 20 years, 592 Swedish men out of 1,465 (21,978 person-years) had died by the end of the follow-up period (Table 2, Albin et al. 1990a).

Determination of Cause of Death and Diagnosis of Lung Cancer/Mesothelioma Cases

Cause of death was determined from death certificates coded according to the eighth revision of the International Classification of Diseases (ICD) by the National Swedish Central Bureau of Statistics. Additionally, all histopathological material was reviewed for respiratory cancers and additional information was collected from necropsy protocols. Mesotheliomas were classified according to the 1982 World Health classification of lung carcinomas. For 12 cases, sufficient material for immunohistochemical examination was also available.

Reference Population

A reference cohort was formed by combining sub-cohorts from five different industries in the region that did not process asbestos. Those industries were fertilizer production, slaughter house, wool and polyester textile, sugar refinery, and metal industries. A total of 1,552 workers composed this group. Of those workers, 142 were excluded from the analysis based on suspected exposure to asbestos in jobs held as electricians, carpenters, repairmen, bricklayers, and firemen. Immigrant workers were also excluded, so the final reference cohort was composed of 1,233 Swedish men. Vital status for the reference cohort was determined in the same manner as for the exposed cohort, and 0.2% of the reference cohort was lost to follow-up. In comparison with the exposed cohort described above, 279 referents with a minimum latency of 20 years out of 762 (10,910 person-years) had died by the end of the follow-up period (Table 2, Albin et al. 1990a).

Estimating Exposure Concentration

For the time period 1956-1969, only midget impinger and gravimetric dust measurements were collected at the Swedish plant. Beginning in 1969, the membrane filter method was used. Estimates of dust concentration for different jobs and periods were made from available information on dust concentrations, production, and dust control. Due to insufficient information for the early period, estimates made for the period from 1947 to 1951 were applied to the entire period prior to 1942. Estimates for the period from 1942 to 1945 were adjusted to account for reductions in asbestos use during that time. The authors do not specifically explain the procedure used for estimating exposures prior to 1956. The median exposure intensity was reported to be 1.2 f/ml for the exposed cohort. Albin et al. (1990a) estimated that the assignments of dust concentrations for the period from 1942 to 1977 were on average likely to be accurate within a factor of two. Although the authors did note that they may have underestimated dust concentrations for some workers in dustier operations such as milling, mixing, sawing, and grinding. The authors specifically state that they did not adjust for higher concentration estimates (approximately 30%-50% higher) prior to 1978 due to the current filter preparation and fiber counting rules in place at the time.

The authors stated that they converted particle-based measures of concentration (mppcf) to estimates of PCM concentration (f/cc) for each job assignment and time period using factors that were comparable to another Swedish cement factory. Factors tended to range from 0.1 to 0.4 in recent years, but appear to have been somewhat higher in the past:

Job	1956 mppcf	f/cc	cf	1956 mppcf	f/cc	cf	1975 mppcf	f/cc	cf
Milling	6.7	6	0.90	11	5	0.45	4.5	1.7	0.38
Mixing	5.5	3	0.55	3	0.3	0.10	5	1.3	0.26
machine line		1.5		2	0.3	0.15	2.3	0.9	0.39
Sawing	2.8	4	1.43	9	1.7	0.19	4.5	1.2	0.27
Grinding	0.7	6.3	9.00	9			4	1.5	0.38

The authors did not attempt to account for differences resulting from changes over time in methods used for filter preparation and counting.

Estimating Cumulative Exposure

Cumulative exposure estimates were based on division among five job categories based on available information from work histories. However, work histories could not be obtained for 22% of the workers, and only incomplete records could be obtained for some others. High exposures occurred during the unloading and storing of asbestos bags and during certain other unspecified jobs. These tasks were not accounted for as they could not be related to individual workers.

Smoking Data

Albin et al. (1990a) did not report any data on smoking habits in the exposed cohort. Albin et al. (1990b) stated that smoking habits were known for 66 (99%) of the asbestos cement workers and 64 (72%) of the reference cohort, but incidence values were not provided.

Lung Cancer Results

Albin et al. (1990a) reported lung cancer mortality for the exposed cohort and the reference cohort for three categories of cumulative exposure. These were computed based on Poisson regression with control for age and calendar year. Data reported in Table 4 of Albin et al. (1990a) for "respiratory disease except mesothelioma" are presented in Figure A12-1. The corresponding ICD code(s) for this mortality classification was not reported. These data were reported as relative risks for each group of workers assigned according to cumulative exposure. Ten total lung cancer deaths were reported in the referent population, compared to 27 total lung cancer deaths reported in the exposed population. The number of observed deaths for each cumulative exposure group is not reported by the authors, but it is possible to allocate the 27 reported deaths based on the ratio of person-years in each exposure group to the total number of person-years reported across all exposure groups (17,028 person-years). As seen, there is no apparent trend in relative risk as a function of increasing dust exposures.

Mesothelioma Results

Thirteen mesotheliomas were identified among exposed workers and one in the referent population. Albin et al. (1990a) stated that there was a highly significant dose-response relation between mortality from pleural mesothelioma and duration of employment, with a 10.4% increase in incidence per year of employment. The same was true for dose (expressed as f/cc-yrs). However, data were not reported in a way that allowed exposure to be expressed in terms of C·Q as needed for the mesothelioma model fitting effort, so these data were not retained for use in this effort.

Uncertainty and Bias Characterization

Appendix C discusses the primary sources of uncertainty in epidemiological studies of cancer risk from asbestos exposure in the workplace and describes the methods used in this document for characterizing the uncertainty. The following sections discuss the uncertainty characterization for this study.

Uncertainty Due to Measurement Error

As described in Section 3.1 of Appendix C, all estimates of concentration levels of asbestos in the workplace are uncertain due to the combination of sampling error and analytical error. These measurements are usually averaged according to job or work area, often stratified by time. For this study, Albin et al. (1990a) report mean concentrations as a function of time period and operation (see Table 1 in the original report). The magnitude of the uncertainty in the reported mean value for each job/time category (which is used to compute cumulative exposure) is a function of a) the number of samples used to compute the mean, b) the between-sample variability, and c) the nature of the underlying distribution. However, the authors do not provide information on the number of samples collected, or on the degree of between-sample variability. Therefore, in the absence of data, the default assumption described in Appendix C is applied to this study to account for measurement error, and is characterized as:

PDF(measurement error) ~ TRI(0.6, 1, 1.5)

Uncertainty in Mean Values for Exposure Groups

The authors report cumulative exposure values as ranges for three of the four exposure groups. One exposure group was composed of referents that had no known exposure to asbestos. For the two exposure groups with bounded ranges, the mid-point of the range is taken as the point estimate. As discussed in Appendix C, this point estimate is an uncertain estimate of the true mean, and the uncertainty is characterized as follows:

PDF(exposure, bounded) ~ TRI(Min/Mid, 1, Max/Mid)

The highest exposure group was reported as an unbounded range (≥ 40 f/cc-yr). As discussed in Appendix C, the point estimate and uncertainty in this case is modeled as:

PDF(exposure, unbounded) ~ TRI(1, 5/3, 3)

Uncertainty in Conversion Factor (CF) from Dust Data (mppcf) to PCM f/cc

In this study, workplace air measurements were available for the period from 1956-1977. However, the membrane filter method was not used until 1969. The conversion of previous dust levels (mppcf) into units of PCM f/cc was based on conversion factors established in a different factory. Details of the derivation of these factors are not presented, so it is difficult to judge the uncertainty in the values that were used. In the absence of additional data, the uncertainty around each operation-specific CF value is assumed to be characterized by about 10% error, as follows:

PDF(conversion factor) ~ TRI(0.9, 1, 1.1)

Uncertainty in the Use of Stationary Rather Than Personal Air Monitors

Personal samplers were used to collect asbestos air measurements in the Swedish plant for all time periods sampled except for collecting total dust measurements in 1956 (Table 1, Albin et al. 1990a). The author's suggest that the predominance of stationary sampling in earlier periods interpreted without accounting for time weighted averages may explain the differences in higher concentrations seen at cement plants in Ontario and Denmark compared to those seen at the Swedish plant. Since personal air monitors were primarily used at this facility, no uncertainty factor is applied to this study to account for the use of stationary air monitors.

Uncertainty in Temporal Representativeness

As noted above, the data used to estimate concentration values in the Swedish plant, which operated from 1907 to 1978, were collected at the plant for the period 1956 to 1977. Albin et al. (1990a) stated that estimates for earlier periods was based on averages over a five year period of data on dust concentrations, production, and dust controls. Insufficient information was available for the before 1942. Assuming similar conditions, the estimates for the period from 1947 to 1951 were used for the whole period prior to 1942. As discussed in Appendix C, when data are considered to only be moderately representative over time, uncertainty is considered to be medium and is characterized as follows:

PDF(temporal representativeness) ~ TRI(0.8, 1, 1.2)

Bias Correction Factor for Data Reported as CE Rather Than CE10

This study reports cumulative exposure as CE rather than as CE10. As discussed in Appendix C, use of CE rather than CE10 tends to bias results low, with the magnitude depending on the duration of exposure, the length of follow-up, and whether or not early person years of observation were excluded. Albin et al. (1990) does not report the average duration, but based on available information on average exposure level (2.5 f/cc) and typical cumulative exposure level (about 37 f/cc-yrs), an average duration of 15 years was estimated. Follow-up ended in 1986, and the average time since last exposure was estimated to be 44 years. The mortality data reported by Albin et al. (1990) are based on a minimum latency of 20 years. Based on these study attributes, the BCF for this cohort was estimated as described in Appendix C, with the following results:

BCF ~ TRI(1.05, 1.08, 1.13)

Uncertainty in Fraction Amphibole

As noted above, the Swedish plant is characterized as having used primarily chrysotile asbestos (>95%) with “smaller amounts” of crocidolite and amosite used during specified periods of time. Albin et al. (1990) states that crocidolite amounts used never exceeded 3-4% of the total asbestos used. Amosite was only used for a few years and the authors state that the maximum total use was less than 18% of the total asbestos use. Based on the information above, the uncertainty distribution around the point estimate for f_{amph} of 2% is characterized by:

$$PDF(f_{amph}) \sim TRI(0, 0.02, 0.05)$$

Uncertainty in Particle Size Data for Chrysotile

As mentioned above, the cement manufacturing plant evaluated by this study used primarily chrysotile asbestos and "small amounts" of amphibole asbestos. Of the TEM data sets available (see Appendix B), 11 are based on chrysotile asbestos. Three of these data sets correspond to the industry of cement pipe manufacturing. These data sets differ by operation as mixing, forming, and finishing. Since Albin et al. (1990a) does not categorize exposure groups by operation, there is no basis to select one TEM data set over the other. Therefore, the three chrysotile data sets based on cement pipe manufacturing were combined. Since the assigned TEM data sets match on asbestos type and industry, the uncertainty in f_{size} for chrysotile is determined to be low for each cohort, and is modeled as follows:

$$PDF(f_{size[chrysotile]}) \sim TRI(0.8, 1, 1.2)$$

Uncertainty in Particle Size Data for Amphibole

For this study, both crocidolite and amosite asbestos were used in small amounts. Of the TEM data sets available (see Appendix B), 18 are based on amphibole asbestos. Three of these data sets are based on crocidolite asbestos for the industry of cement pipe manufacturing. These three data sets differ based on operation (mixing, forming, and finishing), all of which were performed in the Swedish plant. None of the TEM data sets match on both amosite and the cement manufacturing industry. There are five TEM data sets based on amosite asbestos, two for the mining industry, and three for pipe insulation manufacturing. The five data sets based on amosite asbestos were combined with the three crocidolite data sets based on the cement manufacturing industry and applied to this study. As described in Appendix C, if TEM data sets are available that match on mineral form and industry, the uncertainty in f_{size} for amphibole is determined to be low. However, if the TEM data sets match on mineral form and not industry, the uncertainty is determined to be medium. As both of these categories apply to this study, the uncertainty in f_{size} for amphibole is determined to be medium for this cohort, and uncertainty in f_{size} is modeled as follows:

$$PDF(f_{size[amphibole]}) \sim TRI(0.5, 1.0, 1.5)$$

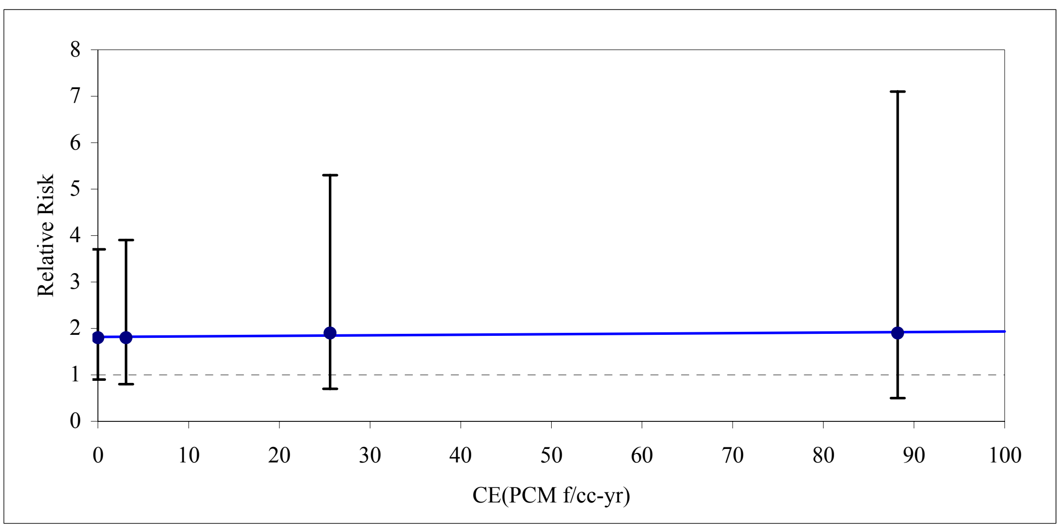
Figure A12-1. Raw Lung Cancer Data for the Swedish Cement Manufacturing Plant

CE(PCM f/cc-yr)		Observed	Expected	Relative Risk (a)		
Range (a)	Mean (a)	Deaths (b)	Deaths (c)	Mean	95% CI	
0	0	10	5.56	1.8	0.9	3.7
0-15	3.1	19	10.6	1.8	0.8	3.9
15-39	25.6	5	2.6	1.9	0.7	5.3
>=40	88.2	3	1.6	1.9	0.5	7.1

a) Data reported in Table 4 (Albin et al. 1990). The relative risk for the referent group (CE=0 PCM f/cc-yr) reported in Table 2 as a point estimate for both those workers exposed to asbestos cement and the referents.

b) The observed number of deaths is reported for the referent group (CE=0 PCM f/cc-yr). The observed numbers of deaths for the exposed groups were calculated based on the ratio of person-years for an exposure group and total person-years across all exposure groups to sum to the total reported lung cancer deaths (27 deaths, 17,028 person-years).

c) Calculated value (observed deaths/relative risk).



A13. Libby, Montana Vermiculite Mine

References

Primary: McDonald, J. C., Harris, J., and Armstrong, B. (2004). Mortality in a cohort of vermiculite miners exposed to fibrous amphibole in Libby, Montana. *Occupational and Environmental Medicine*, **61**: 363-366.

McDonald, J. C., McDonald, A. D., Armstrong, B., and Sebastien, P. (1986). Cohort study of mortality of vermiculite miners exposed to tremolite. *British Journal of Industrial Medicine*, **43**: 436-444.

Other: Amandus, H. E., and Wheeler, R. (1987a). The morbidity and mortality of vermiculite miners and millers exposed to tremolite-actinolite: Part I. Exposure estimates. *American Journal of Industrial Medicine*, **11**: 1-14.

Amandus, H. E., and Wheeler, R. (1987b). The morbidity and mortality of vermiculite miners and millers exposed to tremolite-actinolite: Part II. Mortality. *American Journal of Industrial Medicine*, **11**: 15-26.

Corn, M. and Esmen, N.A. (1979). Work place exposure zones for classification of employee exposures to physical and chemical agents. Journal of the American Industrial Hygiene Association, **40**: 47-57.

Sebastien, P. (1983). Analysis by analytical transmission electron microscopy of fibrous particles in Libby's air samples. Preliminary results. Letter report from P Sebastien (McGill University) to H. A. Eschenbach (W.R. Grace and Co.), June 10, 1983.

Study Description

Location and Facility Description

The site is located in Libby, Montana. The mine is an open-pit vermiculite mine that began limited operations in 1923 and increased rapidly between 1940 and 1950. A dry mill began operation in 1935 and a wet mill began operating in 1950.

Asbestos Type

The vermiculite deposits at the Libby vermiculite mine are contaminated with amphibole asbestos. For many years this asbestos was characterized as belonging to the actinolite/ tremolite series (McDonald et al. 1986, Amandus, H. E., and Wheeler, R. 1987a, 1987b). However, electron microprobe studies by Sebastien et al (1983) and more recently by the United States Geological Survey (USGS) have determined that the amphibole asbestos present in the mine is a mixture of mineral forms, the most common of which are richterite and winchite, which are closely related to actinolite and tremolite. As a result of these findings, the U.S. Environmental Protection Agency (EPA) uses the term "Libby Amphibole" (LA) to describe the mixture of amphibole asbestos present at Libby.

Fraction Amphibole

Based on the absence of chrysotile fibers observed in samples of ore from the mine, the fraction amphibole in the workplace atmosphere is estimated to be 100%.

Cohort Description and Follow-up

Two studies of workers exposed at the Libby site have been reported. Amandus and Wheeler (1987) reported on a cohort of 575 workers hired prior to 1970 who were employed for at least one year. Follow-up was through December 31, 1981. McDonald et al. (1986) performed an overlapping study of the same workforce. This cohort consisted of 406 men hired before 1963 who had a net period of work of at least one year. This cohort was initially followed up through 1983 by McDonald et al. (1986), and follow-up was extended through 1998 by McDonald et al. (2004). The report by McDonald et al. (2004) is preferred for use in this data fitting effort because of the extended period of follow-up.

Determination of Cause of Death and Diagnosis of Lung Cancer/Mesothelioma Cases

Cause of death was identified from death certificates obtained through the National Death Index in the U.S. Certificates were obtained for 99% of the 165 deaths occurring before July 1983. For these cases, cause of death was coded by a certified nosologist according to the eighth revision of the International Classification of Diseases (ICD). The 120 deaths occurring after this period were coded by the State nosologists according to the ninth revision of the ICD. While there are minor differences between the eighth and ninth revisions of the ICD, the authors note that these differences did not affect the distribution by the main certified cause of death between the two periods.

Reference Population

Expected mortality for the main cause death was based on national death rates. In addition, expected mortality based on respiratory cancers was based on white males in the state of Montana.

Estimating Exposure Concentration

Exposure estimates made by McDonald et al. (2004) were the same as those described previously in their 1986 report. Air measurements using the midget impinger method were collected in the dry mill during 1944, 1956, 1958, 1962, and 1969. Measurements after 1969 were performed using the membrane filter method. A total of 1,363 samples were available for the period prior to 1975. Samples were sparse in the earliest time period (only 48 environmental measurements were collected prior to 1965), with 385 for the period 1965-1969, and 903 for the period 1970-74. Both static and personal sampling were used, although McDonald et al. (1986) do not stratify the results by sampling type.

Prior to 1965, dust concentrations were high (geometric mean = 38.9 mppcf). In 1965, installation of a new exhaust fan reduced dust levels by a factor of about 4.6 (8.5 mppcf). No indication of further decreases in concentration after 1965 were identified, so concentrations after 1965 were assumed to be constant. Measurements by membrane filters in 1970 and 1972 showed a mean concentration of 22.1 f/cc. This corresponds to a conversion factor of about 2.6. Therefore, concentrations prior to 1965 were assumed to have been about 1.01 f/cc (4.6 times higher than after 1965). Based on personal air samples, sweepers in the dry mill were assumed to be exposed to concentrations about 20% higher.

Estimating Cumulative Exposure

Individual cumulative exposure estimates (f-y/ml) were computed from job-specific exposure estimates and work histories (McDonald et al. 1986). Estimates were made from first employment to the end of 1982. The authors used a “modified version of the exposure zone concept” (Corn and Esmen 1979) to estimate worker exposures. Operation locations were divided in to 28 categories, and cumulative exposures for each worker were calculated based on job descriptions available from work history files. The operation locations were designed to allocate all available air measurements. Information on location was used to classify static samples, and personal samples were classified by operation. Additionally, information was incorporated into the estimates from interviews with long-term employees concerning changes in processes or control practices.

Smoking Data

Smoking information was not available in McDonald et al. (2004). However, in a parallel study, information on smoking habits was available for men employed between 1975 and 1982 and with at least 5 years of tenure (Amandus and Wheeler 1987). The proportion of these workers who smoked (current or former) was 84% compared to 67% among U.S. white males during the same time period.

Lung Cancer Results

Data for respiratory cancer (assumed to correspond to ICD 162) are presented in Table 3 of McDonald et al. (2004). Exposure is expressed in terms of f/cc-yrs, lagged by 10 years. These data are presented below in Figure A13-1. As seen, lung cancer mortality in this cohort exhibited a significant positive exposure-response trend.

Mesothelioma Results

Twelve mesothelioma deaths were reported for this cohort, four prior to 1983 and eight since 1983. The diagnoses on death certificates were reviewed by McDonald et al. (2004). The authors concluded that nine cases were correctly coded as pleural and peritoneal mesotheliomas (seven and two respectively), and thee cases reported as "site unknown" or pneumoconiosis were actually mesothelioma. The number of cases was provided as a function of cumulative exposure expressed a f/cc-yrs, but data were not provided on mesothelioma incidence as a function of cumulative exposure expressed in terms of C·Q. Therefore, these data were not retained for use in the quantitative fitting of the mesothelioma risk model.

Uncertainty and Bias Characterization

Appendix C discusses the primary sources of uncertainty in epidemiological studies of cancer risk from asbestos exposure in the workplace and describes the methods used in this document for characterizing the uncertainty. The following sections discuss the uncertainty characterization and issues of potential bias for this study.

Uncertainty Due to Measurement Error

As described in Section 3.1 of Appendix C, all estimates of concentration levels of asbestos in the workplace are uncertain due to the combination of sampling error and analytical error. These measurements are usually averaged according to job or work area, often stratified by time. For this study, McDonald et al. (1986) report mean concentrations as a function of time period and job category (see Table 2 in the original report). The magnitude of the uncertainty in the reported mean value for each job/time category (which is used to compute cumulative exposure) is a function of a) the number of samples used to compute the mean, b) the between-sample variability, and c) the nature of the underlying distribution. McDonald et al. (1986) report that prior to 1975, 1,363 air measurements were collected at the Libby mine and mill. However, the authors do not provide information on the degree of between-sample variability. Therefore, in the absence of data, the default assumption described in Appendix C is applied to this study to account for measurement error, and is characterized as:

PDF(measurement error) ~ TRI(0.6, 1, 1.5)

Uncertainty in Mean Values for Exposure Groups

The authors report cumulative exposure as ranges for three of the four exposure groups. For the three exposure groups with bounded ranges, the mid-point of the range is taken as the point estimate. As discussed in Appendix C, this point estimate is an uncertain estimate of the true mean, and the uncertainty is characterized as follows:

PDF(exposure, bounded) ~ TRI(Min/Mid, 1, Max/Mid)

The highest exposure group is characterized by an unbounded range (≥ 113.8 f/cc-yr). As discussed in Appendix C, the point estimate and uncertainty in this case is modeled as:

PDF(exposure, unbounded) ~ TRI(1, 5/3, 3)

Uncertainty in Conversion Factor (CF) from Dust Data (mppcf) to PCM f/cc

As described above, McDonald et al. (1986) utilized a site-specific conversion factor of about 2.6. Because the details of the dust and filter measurements utilized to derive this ratio were not reported, it is difficult to estimate the magnitude of the uncertainty in the factor. A more detailed evaluation of the conversion factor at this site was provided by Amandus et al. (1987a). Based on 336 impinger samples collected between 1965-1969 and 81 filter samples collected between 1967-1971, the ratio of the averages was 33.2 / 8.4 = 4.0 PCM s/cc per mppcf, and this ratio was used by Amandus and Wheeler (1987a) to calculate cumulative exposures. Ratios from other time intervals varied substantially, with most values ranging from about 2 to 8 (see Table V in Amandus and Wheeler

1987a), with a point estimate of 4.0. Based on this, uncertainty in the site-specific CF for this cohort is modeled as:

PDF(conversion factor) ~ TRI (2, 4, 8)

Because the authors selected a value of 4.0 for use, the uncertainty in cumulative exposure attributable to uncertainty in the conversion factor may be modeled as:

PDF(conversion factory) ~ TRI (2,4,8) / 4 = TRI(0.5, 1, 2)

Uncertainty in the Use of Stationary Rather Than Personal Air Monitors

Prior to 1965, all data were collected using dust impingers, which are stationary sampling devices. McDonald et al. (1986) report that both static and personal air monitors were used for collecting air measurements from before 1965 through 1976. However, the authors do not provide details on the relative fraction of samples collected by each approach. In the absence of more detailed data, and recognizing that the highest exposures occurred in the past when only stationary monitors were in use, it is assumed that the measurements collected by the stationary air monitors constituted a majority of the available air measurements. As described in Appendix C, data collected using stationary monitors may tend to underestimate personal air exposures, especially for individuals who actively disturb the asbestos-containing material. Based on this, uncertainty in cumulative exposure due to the use of stationary area monitors is characterized as:

PDF(personal vs. stationary) ~ BETA(2, 20, 0.9, 10)

Uncertainty in Temporal Representativeness

As noted above, intermittent measurements of dust levels were performed between 1944 and 1965, when sampling frequency began to increase. The cohort evaluated by McDonald et al. (2004) was first employed before 1963, so samples are available for the majority of the exposure period. As discussed in Appendix C, when environmental data are considered to be fairly representative of the exposure period, uncertainty is considered to be low and is characterized as follows:

PDF(temporal representativeness) ~ TRI(0.9, 1, 1.1)

Bias Correction Factor for Data Reported as CE Rather Than CE10

This study reports cumulative exposure as CE rather than as CE10. As discussed in Appendix C, use of CE rather than CE10 tends to bias results low, with the magnitude depending on the duration of exposure, the length of follow-up, and whether or not early person years of observation were excluded. McDonald et al. (1986) reported that the average duration of employees at the Libby mine was 8.7 years. Follow-up ended in 1998, and the average time since last exposure was estimated to be 55 years. The mortality data presented by McDonald et al. (2004) is based on the exclusion of the first 10 years of follow-up. Based on these study attributes a BCF for this cohort was estimated using the approach described in Appendix C to be:

BCF ~ TRI(1.1, 1.15, 1.2)

Uncertainty in Fraction Amphibole

Mineralogical studies at the Libby mine have shown the vermiculite deposits in the mine are contaminated with asbestiform amphiboles including minerals in the tremolite-actinolite series, as well as rincherite and winchite. No evidence for the occurrence of chrysotile in the mine has been reported, and chrysotile is not expected to occur as a contaminant of amphibole. Thus, the point estimate for f_{amph} is equal to 1.0 and an uncertainty distribution is not specified.

Uncertainty in Particle Size Data for Amphibole

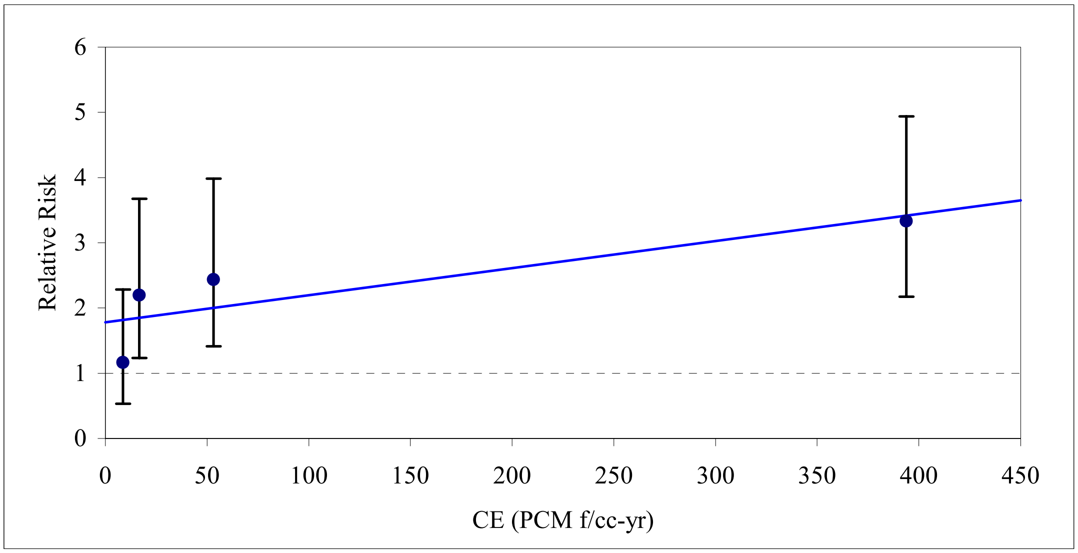
The data set applied to this cohort is based on the study by Sebastien et al. (1983) who analyzed three samples collected from the Libby mill. Since the TEM data are based on the same site as the epidemiological data, uncertainty in the representativeness of the data set is minimal. However, the data are based on a relatively small number of particles (a total of 223), so the fraction of particles in each bin are less certain than for studies with higher numbers of particles. Based on this statistical uncertainty, the uncertainty around f_{size} (amphibole) is ranked as low and the distribution selected for the particle size data for this site is:

PDF($f_{size[amphibole]}$) ~ TRI(0.8, 1.0, 1.2)

Figure A13-1. Lung Cancer Data for Libby, Montana

CE (PCME f/cc-yr)		Observed Deaths (a)	Expected Deaths (a)	Relative Risk		
Range (a)	Mean (a)			Pt. Est.	5% LB	95% UB
0-11.7	8.6	5	4.3	1.2	0.5	2.3
11.7-25.2	16.7	9	4.1	2.2	1.2	3.7
25.2-113.8	53.2	10	4.1	2.4	1.4	4.0
113.8+	393.8	16	4.8	3.3	2.2	4.9

a) Data reported in Table 3 (McDonald et al. 2004).



A14. Wittenoom Australia Crocidolite Miners

References

Primary: de Klerk, N. H., Armstrong, B. K., Musk, A. W., and Hobbs, M. S. (1989). Cancer mortality in relation to measures of occupational exposure to crocidolite at Wittenoom Gorge in Western Australia. *British Journal of Industrial Medicine*, **46**: 529-536.

Other: de Klerk, N. H., Musk, A. W., Armstrong, B. K., and Hobbs, M. S. (1991). Smoking, exposure to crocidolite, and the incidence of lung cancer and asbestosis. *British Journal of Industrial Medicine*, **48**: 412-417.

de Klerk, N. H., Musk, A. W., Armstrong, B. K., and Hobbs, M. S. T. (1994). Diseases in miners and millers of crocidolite from Wittenoom, Western Australia: A further follow-up to December 1986. *Annals of Occupational Hygiene*, **38**(S1): 347-355.

Armstrong, B. K., de Klerk, N. H., Musk, A. W., and Hobbs, M. S. (1988). Mortality in miners and millers of crocidolite in Western Australia. *British Journal of Industrial Medicine*, **45**: 5-13.

Berry, G., de Klerk N.H., Reid, A., Ambrosini, G.L., Olsen, N.J., Merler, E., and Musk, A.W. 2004. Malignant and pleural mesothelioma in former miners and millers of crocidolite in Wittenoom, Western Australia. Occup. Environ. Med. 61.

Rogers A, Majors G. 2002. Letter to the Editor: The Quantitative Risk of mesothelioma and Lung cancer in Relation to Asbestos Exposure: The Wittenoom Data. Arch. Occup. Hyg. 46:127-129.

Study Description

Location and Facility Description

The mine and mill is located at Wittenoom in the Pilbara region of Western Australia. Mining of crocidolite began in 1937 and continued through 1966. From 1943 a single company (the Australian Blue Asbestos Company) managed mining activities carried out by over 6000 employees.

Asbestos Type

Crocidolite asbestos was mined at this location.

Fraction Amphibole

No detailed data on the mineral composition of asbestos from the Wittenoom mine were reported. In the absence of any discussion of the presence of chrysotile, it is assumed the fraction amphibole is 100%.

Cohort Description and Follow-up

The cohort evaluated by de Klerk et al. (1989) is comprised of 6,506 male workers employed between 1943 and 1966. For the most part, duration of employment at the Wittenoom mine and mill was short, with 45% of the men working for less than 3 months, and less than 3% working for five years or longer (Berry et al. 2004). The average durations reported for the cases and controls evaluated by de Klerk et al. (1989) were 1.9 years and 1.2 years, respectively. The authors noted that this cohort was unique in that it offered the opportunity to study the effects of a short period of intense exposure to crocidolite alone, since few employees had other asbestos exposure and most stayed in Wittenoom.

Follow-up was through 1980. Vital status was determined for 73.2% of the employees by the end of the follow-up period. A more recent study (de Klerk et al. 1994) extended follow-up through 1986, although the data in this follow-up report did not stratify the data in a way to allow for use in the quantitative fitting effort.

Determination of Cause of Death and Diagnosis of Lung Cancer/Mesothelioma Cases

De Klerk et al. (1989) did not explicitly discuss the determination of vital status, but Armstrong et al. (1988) reported that vital status was determined from death registries in all states of Australia. Supplemental information was obtained from the Perth Chest Clinic and the Western Australia Mineworkers Relief Fund. Records from the Perth Chest Clinic included chest x-ray examinations.

Reference Population

The study by de Klerk et al. (1989) was a case-control analysis. The cases were 92 men who died from cancer of the trachea, bronchus, and lung, and 31 from malignant mesothelioma. Separate analyses were carried out for each of these diseases. The controls were matched by age and included men who were not known to have died before the date of death of the index case. If possible, up to 20 controls were randomly chosen.

Estimating Exposure Concentration

Armstrong et al. (1988) reported that measurements of dust concentration in air at the mine and mill were made periodically between 1948 and 1958. Results were expressed as dust particles per cubic centimeter (ppcc). Values often exceeded the upper measurement limit of 1000 ppcc. In 1966, concentrations of crocidolite fibers longer than 5 um were measured for 87 job categories in the various work sites. The analysis technique was not stated. Samples were collected using a Casella long running thermal precipitator. Concentration values ranged from 20 f/cc in the mine to 100 f/cc in the mill. Information provided by a former superintendent of operations of Wittenoom regarding the relative environmental conditions were verified by the industrial hygienist who conducted the 1966 survey. This information was used to estimate fiber concentrations in earlier periods and in jobs not covered by the survey.

The accuracy of the workplace measurements used by DeKlerk et. al has been challenged by Rogers and Majors (2002), who feel there is insufficient exposure information to calculate asbestos doses in a scientific manner, and that the values used are at best "guestimates" that are probably too low (which would result in an overestimation of potency).

Estimating Cumulative Exposure

The location, duration and years of exposure were based on information provided in employee records. For incomplete records, information was supplemented by records from the Western Australian Mineworkers Relief Fund, which included information on date of birth, nationality, and dates of employment. The job category information was combined with the estimates of concentration in each area to estimate the exposure level for each subject in the cohort.

Smoking Data

A questionnaire on smoking was sent to 2,928 workers traced as of 1979 (de Klerk et al. 1991). Based on this survey, the incidence of non-smokers was estimated to be 7.5% in the cases (n=40) and 25% in the controls (n=1,799). The proportion of subjects who had stopped smoking more than 10 years before replying to the questionnaire was lower in the controls, whereas the proportion of subjects who had stopped smoking recently or who continued to smoke was greater in the lung cancer cases than in the controls.

Lung Cancer Results

As mentioned above, the case-control study presented by de Klerk et al. (1989) included 92 cases of lung cancer (defined as cancer of the trachea, bronchus, and lung). Table 1 of de Klerk et al. (1989) presents the odds ratio stratified as a function of average exposure concentration (f/cc). For the purposes of this evaluation, the cumulative exposure for each group was estimated by multiplying by the average exposure duration (1.9 years for cases). The odds ratio was used as an estimate of the relative risk. The results are presented in Figure A14-1. As seen, there was an upward trend in relative risk as a function of cumulative exposure, although none of the values were statistically significant.

Mesothelioma Results

de Klerk et al. (1989) reported 31 cases of men with mesothelioma. When evaluated using a case-control approach, there was no statistically significant relationship between the odds ratio for mesothelioma and level of exposure, but there was a significant relationship with time since first employment. There was little indication of a gradient of increasing mortality with duration of exposure. The most recent update followed the Wittenoom cohort up to the end of 2000 (Berry et al. 2004). At this time there were 235 reported cases of mesothelioma in men (202 pleural and 33 peritoneal), and seven in women (all pleural). Most of the cases (92%) occurred after a lag of 20-44 years since first employment. The authors fit the data on number of mesothelioma cases to a model based on cumulative exposure, a lag time, and a lung clearance rate. However, neither de Klerk et al. (1989) nor Berry et al. (2004) provide data on mesothelioma incidence, so these data were not retained for use in the model fitting exercise.

Uncertainty and Bias Characterization

Appendix C discusses the primary sources of uncertainty in epidemiological studies of cancer risk from asbestos exposure in the workplace and describes the methods used in this document for characterizing the uncertainty. The following sections discuss the uncertainty characterization and issues of potential bias for this study.

Uncertainty Due to Measurement Error

As described in Section 3.1 of Appendix C, all estimates of concentration levels of asbestos in the workplace are uncertain due to the combination of sampling error and analytical error. These measurements are usually averaged according to job or work area, often stratified by time. For this study, de Klerk et al. (1989) report mean concentrations for the cases and controls (see Table 1 in the original report). The magnitude of the uncertainty in the reported mean value for each job/time category (which is used to compute cumulative exposure) is a function of a) the number of samples used to compute the mean, b) the between-sample variability, and c) the nature of the underlying distribution. However, the authors do not provide information on the number of samples collected, or on the degree of between-sample variability. Therefore, in the absence of data, the default assumption described in Appendix C is applied to this study to account for measurement error, and is characterized as:

PDF(measurement error) ~ TRI(0.6, 1, 1.5)

Uncertainty in Mean Values for Exposure Groups

In the data used to evaluate lung cancer, exposure concentrations were reported as ranges for three of the four exposure groups. For the three exposure groups with bounded ranges, the mid-point of the range is taken as the point estimate. As discussed in Appendix C, this point estimate is an uncertain estimate of the true mean, and the uncertainty is characterized as follows:

PDF(exposure, bounded) ~ TRI(Min/Mid, 1, Max/Mid)

As discussed in Appendix C, for the highest exposure group with an unbounded range, the point estimate and uncertainty is modeled as:

PDF(exposure, unbounded) ~ TRI(1, 5/3, 3)

Uncertainty in Conversion Factor (CF) from Dust Data (mppcf) to PCM f/cc

Although no details on the analytical methods are reported, all of the concentration values used to estimate exposure were based on fibers longer than 5 um. In the absence of data to the contrary, it is assumed these concentration values were derived using PCM. Therefore, no uncertainty factor for conversion from dust measurements to fiber concentrations is need.

Uncertainty in the Use of Stationary Rather Than Personal Air Monitors

There was no mention of the use of personal air monitors at the Wittenoom mine or mill. In the absence of knowledge, it is assumed the measures were collected using stationary monitors. As discussed in Appendix C, use of stationary monitors may tend to underestimate the true exposure level of workers, especially those engaged in activities that actively disturb asbestos-containing materials or dusts. Based on available data on the ratio of particulate concentrations measured using personal to stationary monitors at various locations, the uncertainty attributable to this source may be characterized as:

PDF(personal vs. stationary) ~ BETA(2, 20, 0.9, 10)

Uncertainty in Temporal Representativeness

As described above, the measurements used by de Klerk et al. (1989) were based on a survey conducted in 1966. Earlier periods were estimated based on information provided by a former employee. As discussed in Appendix C, when use of extrapolated data is predominant, the uncertainty in temporal representativeness is considered to be high and is characterized by:

PDF(temporal representativeness) ~ TRI(0.5, 1, 1.5)

Bias Correction Factor for Data Reported as CE Rather Than CE10

This estimates of exposure used in the evaluation of lung cancer risk are based on CE rather than as CE10. As discussed in Appendix C, use of CE rather than CE10 tends to bias results low, with the magnitude depending on the duration of exposure, the length of follow-up, and whether or not early person years of observation were excluded. de Klerk et al. (1989) report the average duration of employment for the cases as 1.9 years. End of follow-up was1980, and the average time since last exposure was estimated to be 25 years. de Klerk et al. (1989) did not limit data based on latency. Based on these study attributes, a BCF was estimated for this cohort as described in Appendix C as follows:

$$BCF \sim TRI(1.5, 1.8, 3)$$

Uncertainty in Fraction Amphibole

As noted above, only crocidolite asbestos was mined at the Wittenoom mine. Thus, in the absence of any information that trace levels of chrysotile may have been present, the point estimate for f_{amph} is equal to 1.0 and an uncertainty distribution is not specified.

Uncertainty in Particle Size Data for Amphibole

Of the TEM data sets available (see Appendix B), 5 are based on crocidolite asbestos for the mining/milling industry. These data sets differ by operation including mining, bagging, storage, and crushing. There is no basis to assign a distribution based on a single operation to the cohort evaluated by de Klerk et al. (1989). As such, the five crocidolite TEM data sets based on mining/milling were combined and applied to this study. As described in Appendix C, if TEM data sets are available that match on mineral form and industry, the uncertainty in f_{size} for amphibole is determined to be low, and is modeled as follows:

$$PDF(f_{size[amphibole]}) \sim TRI(0.8, 1.0, 1.2)$$

Figure A14-1. Lung Cancer Data for the Australian Mine in Wittenoom

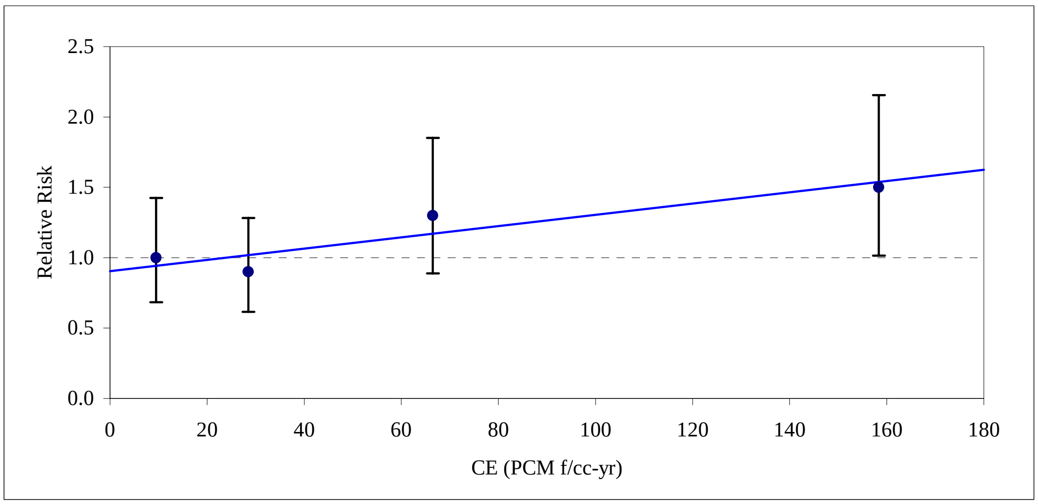
Conc. (f/cc) (a)		Cum Exp (b)	Number of Cases		Odds Ratio (d)		
Range	PE	(f/cc-yrs)	Observed (a)	Expected (c)	Pt. Est. (a)	5% LB	95% UB
0-9.9	5	9.5	20.0	20.0	1.0	0.7	1.4
10-19.9	15	28.5	20.0	22.2	0.9	0.6	1.3
20-49.9	35	66.5	20.0	15.4	1.3	0.9	1.9
>= 50	83.3	158.3	19.0	12.7	1.5	1.0	2.2

a) Data from Table 1 (de Klerk et al. 1989)

b) Point estimate of concentration multiplied by average exposure duration of 1.9 years.

c) Calculated from odds ratio (Expected = observed / odds ratio)

d) Odds ratio is taken to be a reasonable approximation of RR.



A15. Belgian Asbestos Cement Factory

References

Primary: Lacquet LM; van der Linden L, Lepoutre J. 1980. Roentgenographic Lung Changes, Asbestosis and Mortality in a Belgian Asbestos-Cement Factory. In: Biological Effects of Mineral Fibres, Wagner JC (ed.). IARC Sci. Publ. pp. 783–793.

Study Description

Location and Facility Description

The plant is located in Belgium at Kapelle op de Bos. The plant employs about 2000 workers and 400 staff members and processes about 40,000 tons of asbestos annually in the manufacture of asbestos-cement building materials and pipes.

Asbestos Type

Most of the asbestos used at the Belgian plant is chrysotile (about 35,000 tons per year), but about 3,000 tons of crocidolite and 1,000 tons of amosite are also used per year.

Fraction Amphibole

Based on the information on the mass of amphibole asbestos used annually (see above), the point estimate for the fraction of amphibole used at the Belgian plant is 10% (4,000 tons amphibole / 39,000 tons total asbestos used).

Cohort Description and Follow-up

The cohort evaluated by Lacquet et al. (1980) included male workers employed for at least 1 year during the period from 1963 to 1977. This included a total of 1,973 men and 29,366 man-years of observation. The study occurred in 1977 meaning that the follow-up period was concurrent with the employment period.

Determination of Cause of Death and Diagnosis of Lung Cancer/Mesothelioma Cases

Because death certificates are not released in Belgium, the cause of death for deceased workers was checked through family doctors or social workers who visited relatives of the workers.

Reference Population

The expected number of deaths was based on yearly mortality rates for Belgium, available in WHO tables for 1965 to 1975. Data for other years were obtained through extrapolation, although Lacquet et al. (1980) do not provide further detail. In addition, the authors noted that comparing mortality in a worker cohort to national statistics might be questionable. To evaluate this issue and eliminate the "healthy worker effect", Lacquet et al. (1980) also made comparisons using internal case-controls. Four controls were matched to each worker who died from respiratory cancer from men alive at least one year after the case worker had died. The controls were matched to the cases based on age and date of hire at the Belgium plant.

Estimating Exposure Concentration

The workplace was divided into five working areas, as follows:

Area	Description
0	Areas outside the workplace
1	Offices
2	Moulding of asbestos sheets and pipes
3	Finishing of cement products (sawing, drilling, filing, etc.)
4	Handling or milling of asbestos fibers

Fiber counts obtained with the filter-membrane method are available for each type of work area for the period 1970-1976. Dust levels were believed to have been much higher in the past, and were estimated using a logistic decay model of the form:

$$c_y = c_0 / (1 + 1.16^{y-1960})$$

where:

c_y = Concentration of fibers (f/cc) in year y

c_0 = Estimated historic concentration levels (about 10-times higher than 1970-1976 measured levels). Values are 0.4, 16, 24 or 100 f/cc for areas 1, 2, 3 and 4 respectively.

Estimating Cumulative Exposure

Since employees may have worked consecutively in different areas of the Belgian plant, the cumulative exposure of each individual was computed as:

$$CE = \Sigma C_{i,y}$$

where i is the work area and y is the year.

Smoking Data

Lacquet et al. (1980) did not report information on smoking prevalence within the Belgian cohort.

Lung Cancer Results

Observed and expected number of lung cancer deaths for the Belgian cohort, stratified by cumulative exposure, are reported in table 8 of Lacquet et al. (1980). These data are shown in Figure A15-1. Based on the data as reported, mortality from respiratory cancer was not significantly different from that which would be expected in a Belgian population. The 20 deaths from respiratory cancer included three cancers of the upper airways and 17 cancers of the lung. Lacquet et al. (1980) also reported that there was no significant difference between cases and controls with respect to cumulative exposure, which indicated that dust exposure did not significantly affect mortality due to respiratory cancer.

Mesothelioma Results

One pleural mesothelioma was reported in the study. This occurred in the group with the highest cumulative exposure (1600-3200 f/cc-yrs), but data on average duration or time since first exposure were not reported. Therefore, this study was not retained for use in the quantitative fitting of the mesothelioma risk model.

Uncertainty and Bias Characterization

Appendix C discusses the primary sources of uncertainty in epidemiological studies of cancer risk from asbestos exposure in the workplace and describes the methods used in this document for characterizing the uncertainty. The following sections discuss the uncertainty characterization and issues of potential bias for this study.

Uncertainty Due to Measurement Error

As described in Section 3.1 of Appendix C, all estimates of concentration levels of asbestos in the workplace are uncertain due to the combination of sampling error and analytical error. These measurements are usually averaged according to job or work area, often stratified by time. The magnitude of the uncertainty in the reported mean value for each job/time category (which is used to compute cumulative exposure) is a function of a) the number of samples used to compute the mean, b) the between-sample variability, and c) the nature of the underlying distribution. However, Lacquet et al. (1980) do not provide information on the job exposure matrix, the number of samples collected, or on the degree of between-sample variability. Therefore, in the absence of data, the default assumption described in Appendix C is applied to this study to account for measurement error, and is characterized as:

PDF(measurement error) ~ TRI(0.6, 1, 1.5)

Uncertainty in Mean Values for Exposure Groups

Lacquet et al. (1980) report cumulative exposure as ranges for seven exposure groups. All seven exposure groups had bounded ranges, so the mid-point of the range is taken as the point estimate. As discussed in Appendix C, this point estimate is an uncertain estimate of the true mean, and the uncertainty is characterized as follows:

PDF(exposure, bounded) ~ TRI(Min/Mid, 1, Max/Mid)

Uncertainty in Conversion Factor (CF) from Dust Data (mppcf) to PCM f/cc

In this study, workplace air measurements were collected by the membrane filter method from 1970 to 1976. Thus, no conversion factor is needed to account for extrapolation from dust to fiber concentrations.

Uncertainty in the Use of Stationary Rather Than Personal Air Monitors

No details were provided on whether the air measurements utilized stationary or personal air monitors. In the absence of knowledge, it is assumed the measures were collected using stationary monitors. As discussed in Appendix C, use of stationary monitors may tend to underestimate the true exposure level of workers, especially those engaged in activities that actively disturb asbestos-containing materials or dusts. Based on available data on the ratio of particulate concentrations measured using personal to stationary monitors at various locations, the uncertainty attributable to this source may be characterized as:

PDF(personal vs. stationary) ~ BETA(2, 20, 0.9, 10)

Uncertainty in Temporal Representativeness

As noted above, the data used to estimate concentration values in the Belgian plant were collected at the plant from 1970 through 1976. The cohort evaluated by Lacquet et al. (1980) consisted of men who worked at the cement plant during the period from 1963-1977. For the period prior to 1970, Lacquet et al. (1980) estimated dust concentrations based on the assumption of dustier conditions for those years. The authors acknowledge their estimates of past exposures as “good guesses at best”. Thus, the uncertainty is considered to be high for this study and is characterized as follows:

PDF(temporal representativeness) ~ TRI(0.5, 1, 1.5)

Bias Correction Factor for Data Reported as CE Rather Than CE10

This study reports cumulative exposure as CE rather than as CE10. As discussed in Appendix C, use of CE rather than CE10 tends to bias results low, with the magnitude depending on the duration of exposure, the length of follow-up, and whether or not early person years of observation were excluded. Lacquet et al. (1980) does not report the average duration, but based on the person-year weighted average cumulative exposure (156 f/cc-yrs) and the estimated average concentration across the four areas reported by the authors as c_o, an average duration of 4.4 years was estimated. Follow-up ended in 1977, and the average time since last exposure was estimated to be 7 years. The mortality data reported by Lacquet et al. (1980) do not exclude any person years of observation. Based on these study attributes, a BCF was calculated for this cohort as described in Appendix C with the following results:

BCF ~ TRI(2.7, 3.3, 4.5)

Uncertainty in Fraction Amphibole

As noted above, the Belgian plant is characterized as utilizing 35,000 tons of chrysotile annually, along with 4,000 tons of amphibole. Because the information on f_{amph} is based on descriptions of relative mass rather than any direct particles counts in workplace air, and because relative masses may have fluctuated over time, uncertainty around the point estimate of 10% is judged to be moderate, and is characterized as:

$PDF(F_{amph})$ ~ TRI(0.08, 0.10, 0.12)

Uncertainty in Particle Size Data for Chrysotile

Of the TEM data sets available (see Appendix B), 11 are based on chrysotile asbestos. Three of these data sets correspond to the cement pipe manufacturing industry. These data sets differ by operation as mixing, forming, and finishing, all of which occurred at the Belgian plant. The data extracted from Lacquet et al. (1980) is not categorized by operation, so there is no basis to select one TEM data set over the other. Therefore, the three chrysotile data sets based on cement pipe manufacturing were combined and applied to this study. Since the assigned TEM data sets match on asbestos type and industry, the uncertainty in f_{size} for chrysotile is determined to be low for this cohort, and is modeled as follows:

$PDF(f_{size[chrysotile]})$ ~ TRI(0.8, 1, 1.2)

Uncertainty in Particle Size Data for Amphibole

As described above, 3,000 tons of crocidolite and 1,000 tons of amosite were used per year at this site. Of the TEM data sets available (see Appendix B), 18 are based on amphibole asbestos. Three of these data sets are based on crocidolite asbestos for the industry of cement pipe manufacturing. These three data sets differ based on operation (mixing, forming, and finishing), all of which are general operations performed in the Belgian plant. There are five TEM data sets based on amosite asbestos, two for the mining industry, and three for pipe insulation manufacturing. The five data sets based on amosite asbestos were combined with the three crocidolite data sets based on the cement manufacturing industry and applied to this study. As described in Appendix C, if TEM data sets are available that match on mineral form and industry, the uncertainty in f_{size} for amphibole is determined to be low. However, if the TEM data sets match on mineral form and not industry, the uncertainty is determined to be medium. As both of these categories apply to this study, the uncertainty in f_{size} for amphibole is determined to be medium for this cohort, and uncertainty in f_{size} is modeled as follows:

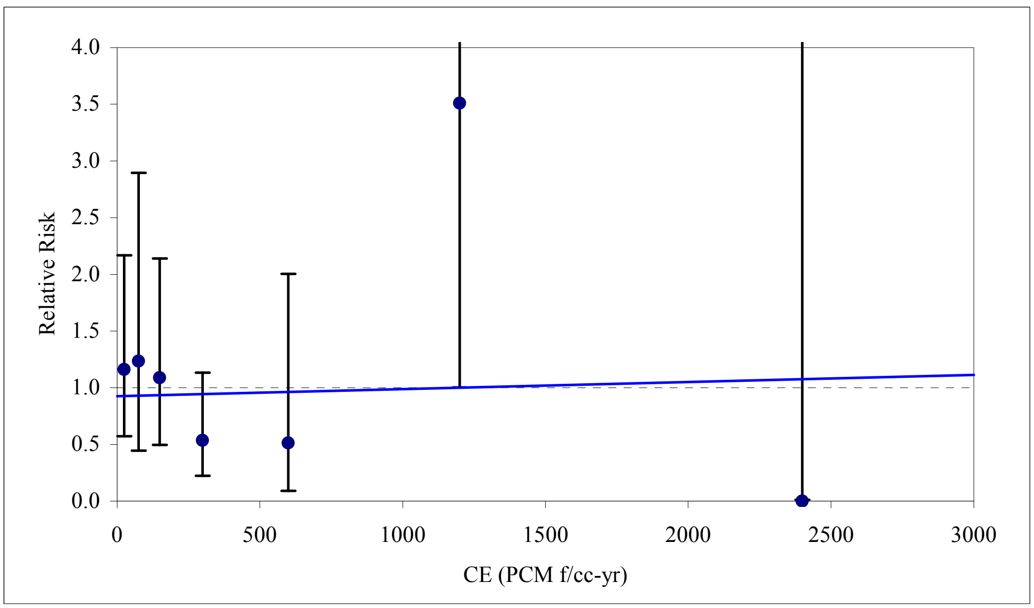
$$PDF(f_{size[amphibole]}) \sim TRI(0.5, 1.0, 1.5)$$

Figure A15-1. Raw Lung Cancer Data for the Belgium Cement Plant

CE (PCM f/cc-yr)		Observed	Expected	Relative Risk		
Range (a)	Mean (b)	Deaths (a)	Deaths (a)	Pt. Est.	5% LB	95% UB
0-49	24.5	6	5.2	1.2	0.6	2.2
50-99	74.5	3	2.4	1.2	0.4	2.9
100-199	149.5	5	4.6	1.1	0.5	2.1
200-399	299.5	4	7.5	0.5	0.2	1.1
400-799	599.5	1	2.0	0.5	0.1	2.0
800-1599	1199.5	2	0.6	3.5	1.0	9.7
1600-3200	2400	0	0.2	0.0	0.0	11.3

a) Data reported in Table 8 (Lacquet et al. 1980).

b) Calculated as the midpoint of the reported range.



A16. Austrian Cement Factory

References

Primary: Nueberger, M. and Kundi, M. (1990). Individual asbestos exposure: smoking and mortality – a cohort study in the asbestos cement industry. *British Journal of Industrial Medicine*, **47**: 615-620.

Other: Neuberger, M. (1979). Neue Wege zur Risikobewertung von Luftschadstoffen. Experimentelle und epidemiologische. Beitrage zu Luftqualitatskriterien fur Kohlenmonoxid und Asbestos. Vienna: Facultas Verlag, p. 47-117.

Nueberger, M., Kundi, M., and Friedl, H-P. (1984). Environmental asbestos exposure and cancer mortality. *Archives of Environmental Health*, **39**: 261-265.

Neuberger, M. and Kundi, M. Zum berufskrebsrisiko durch Asbest in Osterreich. In: 2. Kolloquium zur Beurteilung der Krebsgefahr durch Asbets. Berlin: Bundesgesundheitsamt.

Study Description

Location and Facility Description

The factory is located in Vöcklabruck, Austria. It is the oldest asbestos cement factory in the world. Operations began in 1895 and continued through 1986. Production increased following the Second World War. Asbestos used by the facility was about 28,000 tons in 1973 and 18,000 tons in 1985. Efficient systems for dust removal were not in place until the mid 1960s. In 1975 a new high performance dust removal system was used at this facility.

Asbestos Type

Chrysotile was the predominant form of asbestos used in the Austrian factory. From 1920 to 1977 crocidolite was also used in the pipe factory. From 1970 to 1986 amosite was used for certain products. However, the authors report that the use of amosite played no part in the exposure of the employees.

Fraction Amphibole

The authors of the study do not provide data on the relative amounts of chrysotile and amphibole (crocidolite) used at the plant. The Ontario Royal Commission (1984) stated that crocidolite generally constitutes about 20% of the asbestos used in the pipe process, but the fraction of asbestos used in pipe production (*vs* other cement products that do not contain crocidolite) is unknown. Assuming that pipe production constitutes about half of the cement products produced at the factory, this corresponds to an estimate of about 10% for fraction amphibole.

Cohort Description and Follow-up

The cohort evaluated by Neuberger and Kundi (1990) consisted of 2,816 persons employed for at least three years during the period from 1950 to 1981. Eighty-two percent of the workforce had been employed before 1969 (when conditions improved). Follow-up was carried out until the end of 1986. One hundred and twenty-one persons (4.3%) were lost to follow-up mainly due to emigration. In total, 51,218 person-years were included in the analysis. Most of the persons in the cohort started work in the asbestos cement industry about age 20, but older persons also joined the workforce during periods of high production.

Determination of Cause of Death and Diagnosis of Lung Cancer/Mesothelioma Cases

Cause of death was determined from death certificates with the aid of death registries, physicians, and pathologists. Diagnosis on death certificates in this region of Austria were made on the basis of necropsy in every third case of death. By the end of follow-up, 540 persons were reported to be deceased.

Reference Population

The authors originally intended to use cement workers from another facility that did not use asbestos as the reference population. However, the population size was too small to yield reliable reference statistics, so the authors estimated expected deaths based on mortality rates for the Upper Austrian population.

Estimating Exposure Concentration

Dust measurements from 1965 – 1975 were made mainly by conimeter. For the period after 1975, measurements were taken using personal air samplers and membrane filter methods. Concentrations for the period before 1965 were stated to be estimated, but the details of the estimation procedure were not reported in this publication.

Estimating Cumulative Exposure

Occupational exposures were estimated from 1973 using personal records and standardized questionnaires. Individual records included information on duration of exposure at different workplaces.

Smoking Data

Interviews with employees still alive in 1982 were conducted using a questionnaire on exposures and smoking habits. Smoking histories were available for 2,095 living workers and 433 deceased. Tobacco consumption was higher (52%) in the cohort as compared to the general population from the microcensus for Upper Austria (39%), with even a bigger difference for workers over 40 years old (53% vs. 25%)

Lung Cancer Results

Lung cancer data for Austrian asbestos cement workers are reported in Table 2 of Neuberger and Kundi (1990). These data are presented in Figure A16-1. The expected numbers of cases for each of the two exposure groups are adjusted based on knowledge of smoking habits in the cohort. As seen, a negative dose-response between cumulative exposure and relative risk was observed. A log-linear relation was found between the number of cigarettes smoked each day and the lung cancer death rate. Compared to the general population of the area, lung cancer deaths were significantly higher. Neuberger and Kundi (1990) also reported on the results of an additional analysis investigating the effects of latency. This investigation involved excluding all persons who had not been observed for more than 15 years from start of exposure. This resulted in 42 observed cases of lung cancer compared with 41.82 expected cases (after adjustment for smoking). This corresponds to an SMR of 1.0 (95% CI = 0.71-1.59).

Mesothelioma Results

There were five confirmed cases of mesothelioma in this cohort, four verified by necropsy and histology. The corresponding rates in the general Austrian population were orders of magnitude lower. However, the data were not presented in a form that allowed for use of these data in the quantification of mesothelioma risk.

Uncertainty and Bias Characterization

Appendix C discusses the primary sources of uncertainty in epidemiological studies of cancer risk from asbestos exposure in the workplace and describes the methods used in this document for characterizing the uncertainty. The following sections discuss the uncertainty characterization and issues of potential bias for this study.

Uncertainty Due to Measurement Error

As described in Section 3.1 of Appendix C, all estimates of concentration levels of asbestos in the workplace are uncertain due to the combination of sampling error and analytical error. These measurements are usually averaged according to job or work area, often stratified by time. The magnitude of the uncertainty in the reported mean value for each job/time category (which is used to compute cumulative exposure) is a function of a) the number of samples used to compute the mean, b) the between-sample variability, and c) the nature of the underlying distribution. However, Neuberger and Kundi (1990) do not provide information on the job exposure matrix, the number of samples collected, or on the degree of between-sample variability. Therefore, in the absence of data, the default assumption described in Appendix C is applied to this study to account for measurement error, and is characterized as:

PDF(measurement error) ~ TRI(0.6, 1, 1.5)

Uncertainty in Mean Values for Exposure Groups

Neuberger and Kundi (1990) report cumulative exposure values as ranges for two exposure groups. For the first exposure group (0-25 f/cc-yr), the mid-point of the range is taken as the point estimate. As discussed in Appendix C, this point estimate is an uncertain estimate of the true mean, and the uncertainty is characterized as follows:

PDF(exposure, bounded) ~ TRI(Min/Mid, 1, Max/Mid)

The second group is characterized as an un-bounded bin ((> 25 f/cc-yr). As discussed in Appendix C, the point estimate and uncertainty in this case are modeled as:

PDF(exposure, unbounded) ~ TRI(1, 5/3, 3)

Uncertainty in Conversion Factor (CF) from Dust Data (mppcf) to PCM f/cc

In this study, measurements of dust in workplace air were collected by the conimeter method from 1965 to 1975, and estimates of asbestos concentration were obtained by the membrane filter method for the subsequent period. Since the details of the conversion between these two methods is not provided, it is difficult to estimate the uncertainty that might result. In the absence of additional information, the uncertainty in the conversion is assumed to be moderate and is characterized as follows:

PDF(conversion factor) ~ TRI(0.7, 1, 1.3)

Uncertainty in the Use of Stationary Rather Than Personal Air Monitors

From 1965 to 1975, stationary samplers were used to collect dust measurements at the Austrian cement plant. Beginning in 1975, air measurements were collected using personal air samplers. Stationary air samplers were used to estimate the asbestos concentration in the workplace for over 80% of the exposure period for this cohort (1950-1981). As described in Appendix C, use of stationary monitors may tend to underestimate the true exposure level of workers, especially those engaged in activities that actively disturb asbestos-containing materials or dusts. Thus, the uncertainty in cumulative exposure due to the use of stationary area monitors is characterized as:

PDF(personal vs. stationary) ~ BETA(2, 20, 0.9, 10)

Uncertainty in Temporal Representativeness

As noted above, regular dust measurements began in 1965. The cohort evaluated by this study consisted of persons employed at the Austrian cement manufacturing plant between 1950 and 1981. Thus, air measurements were available for later exposure periods, but were estimated for the 15 years constituting the earlier exposure periods. Thus, as discussed in Appendix C, the uncertainty is considered to be medium for this study and is characterized as follows:

PDF(temporal representativeness) ~ TRI(0.8, 1, 1.2)

Bias Correction Factor for Data Reported as CE Rather Than CE10

This study reports cumulative exposure as CE rather than as CE10. As discussed in Appendix C, use of CE rather than CE10 tends to bias results low, with the magnitude depending on the duration of exposure, the length of follow-up, and whether or not early person years of observation were excluded. Neuberger and Kundi (1990) did not report the average duration, and data are not presented in a form for calculating an average duration. Therefore, an average duration of 8 years was applied to this study as an estimated value with large uncertainty associated. Follow-up ended in 1986, and the average time since last exposure was estimated to be 20 years. As described above, the mortality data grouped by cumulative exposure reported by Neuberger and Kundi (1990) did not exclude person-years based on latency. Based on these study attributes, a BCF was estimated for this cohort using the approach described in Appendix C as follows:

$$BCF \sim TRI(1.5, 1.7, 1.9)$$

Uncertainty in Fraction Amphibole

As noted above, the Austrian plant is characterized as having used primarily chrysotile asbestos. Crocidolite asbestos was also used in the pipe factory from 1920 to 1977. Amosite was also used for certain products from 1970 to 1986, but according to Neuberger and Kundi (1990), amosite did not play a part in employee exposure. Because no data are reported on the relative amounts of amphibole used in the plant, the point estimate of 10% is very uncertain. In the absence of additional information, the bounds on this term are estimated to be as follows:

$$PDF(f_{amph}) \sim TRI(0.05, 0.10, 0.20)$$

Uncertainty in Particle Size Data for Chrysotile

Of the TEM data sets available (see Appendix B), 11 are based on chrysotile asbestos. Three of these data sets correspond to the cement pipe manufacturing industry. These data sets differ by operation as mixing, forming, and finishing. Since Neuberger and Kundi (1990) do not categorize exposure groups by operation, there is no basis to select one TEM data set over the other. Therefore, the three chrysotile data sets based on cement pipe manufacturing were combined. Since the assigned TEM data sets match on asbestos type and industry, the uncertainty in f_{size} for chrysotile is determined to be low for this cohort, and is modeled as follows:

$$PDF(f_{size[chrysotile]}) \sim TRI(0.8, 1, 1.2)$$

Uncertainty in Particle Size Data for Amphibole

Crocidolite and amosite were used in addition to chrysotile asbestos. However, the authors state that amosite played no part in the exposure of the employees. Of the TEM data sets available (see Appendix B), three are based on crocidolite asbestos for the industry of cement pipe manufacturing. These three data sets differ based on operation (mixing, forming, and finishing), all of which are general operations most likely performed in the Austrian plant. There is no basis to select one TEM data set over the other, so these three crocidolite data sets were combined and applied to this study. As described in Appendix C, if TEM data sets are available that match on mineral form and industry, the uncertainty in f_{size} for amphibole is determined to be low, and uncertainty is modeled as:

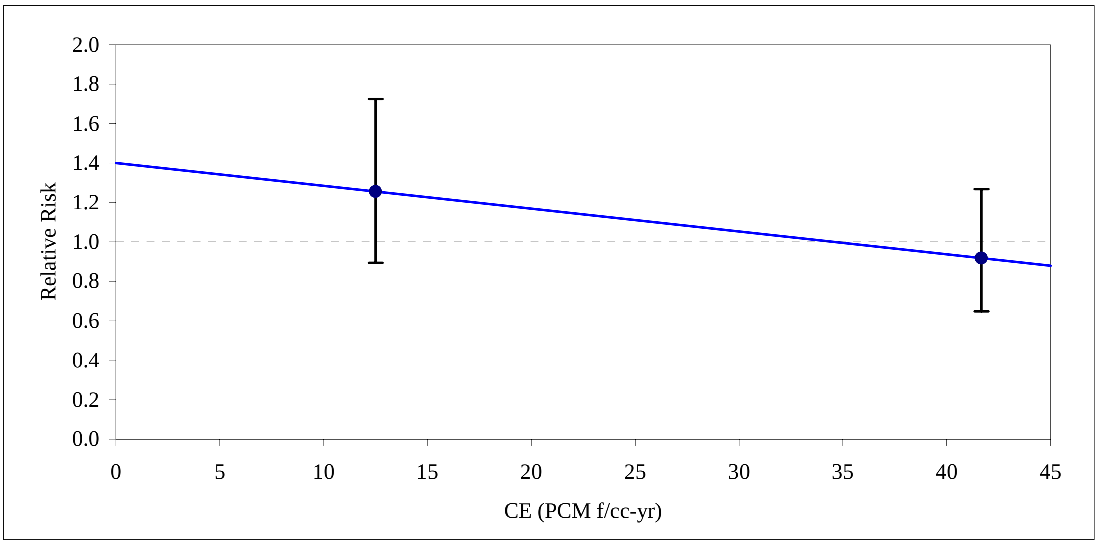
$$PDF(f_{size[amphibole]}) \sim TRI(0.8, 1, 1.2)$$

Figure A16-1. Raw Lung Cancer Data for Austrian Cement Workers

CE (PCM f/cc-yr)		Observed	Expected	Relative Risk		
Range (a)	Mean (b)	Deaths (a)	Deaths (a)	Pt. Est.	5% LB	95% UB
0-25	12.5	25	19.9	1.3	0.9	1.7
>25	41.7	24	26.2	0.9	0.6	1.3

a) Data reported in Table 2 (Neuberger and Kundi 1990).

b) Calculated as the midpoint of the reported range of CE, except for the highest exposure group which has an unbounded range. The point estimate is assigned a value = 5/3*lower bound.



A17. China Asbestos Products Factory

References

Primary: Yano, E., Wang, Z-M, Wang, X-R, Wang, M-Z, and Lan, Y-J. (2001). Cancer mortality among workers exposed to amphibole-free chrysotile asbestos. *American Journal of Epidemiology*, **154**: 538-543.

Other: Tossavainen A, Kotilainen M, Takahasi K, Pan G, Vanhala E. 2001. Amphibole Fibers in Chinese Chrysotile Asbestos. Ann. Occup. Hyg. 45:145-152.

Study Description

Location and Facility Description

The plant is located in Chongqin, China. Operations began in 1939, and since 1958 has expanded substantially in size and in the variety of products produced. In the 1970s, the products manufactured included asbestos-containing textiles, cement products, friction materials, rubber products, and heat resistant materials.

Asbestos Type

Only chrysotile asbestos was used in this plant. The chrysotile was obtained from two mines in Sichuan province, China. In 1996, 6,000 tons of raw chrysotile asbestos was used.

Fraction Amphibole

Yano et al. (2001) examined four commercial samples from the two mines at Sichuan exclusively used in the Chongqin chrysotile plant by x-ray diffraction and TEM. No amphibole asbestos was detected in the samples at a reported detection limit of 0.001%. While it is considered possible that trace levels (of less than 0.001%) might be present, this amount is considered to be negligible, and the fraction amphibole is assumed to be zero. Note, however, that Tossavainen et al. (2001) reported that amphibole fibers were present at levels of 0.006% to 0.31% in 10 bulk chrysotile samples from six mines in China, including four samples from Sichuan province. The basis for this apparent discrepancy between the findings of Yano et al. (2001) and Tossavainen et al. (2001) is not known

Cohort Description and Follow-up

The study was a 25-year longitudinal study. As of January 1972, there were 754 workers actively employed at the Chinese plant, none of which showed any signs of disease. This group included 130 females and 109 males who had only been working for less than one year. These employees were excluded from the cohort. Thus, the final cohort was comprised of 515 male workers (11,525 person-years) employed in January 1972 and who had worked at the plant for longer than one year. Workers employed after January 1, 1972 were not included in the cohort. On average members of this workforce began employment around age 29 and worked for 25 years in the Chinese plant. Follow-up was for 25 years, through December 31, 1996. The average number of years of observation for this cohort was around 34 years. Yano et al. (2001) reports that a majority of the cohort retired during the follow-up period, but remained in company housing and returned to the plant monthly to collect their pension checks. The number of workers that fall in to this group is not reported.

Determination of Cause of Death and Diagnosis of Lung Cancer/Mesothelioma Cases

Vital status was determined annually through personnel records maintained at the plant. These records included information on death, leave, retirement, and development of malignant tumors. Municipal hospitals were also checked for cause of death. For workers who left the plant prior to retirement (20 asbestos workers and 33 controls), vital status was determined through interviewing close friends or relatives. For workers that did retire during the follow-up period, their vital status was maintained as they came in to the plant every month to receive their pension. A total of 132 deaths had occurred in the exposed cohort by 1996. Of these, 50 were from lung cancer and 2 were from mesothelioma. Six of the lung cancer cases were confirmed pathologically, while both mesothelioma cancers were confirmed by pathologic examination.

Reference Population

A control population was based on 1,239 workers at an electronics manufacturing plant located in the suburbs of Chongqin who had no known asbestos exposure. This plant was comparable to the Chinese asbestos plant in terms of socioeconomic, geographic, and working conditions. These workers were followed for the same period as the exposed cohort. None of the workers at this plant showed signs of malignant tumors. Of this cohort, 535 females, 28 male workers with less than one year of employment by January 1, 1972, and 26 workers exposed to workplace dust were excluded. Thus, the reference cohort was comprised of 650 male workers that were followed concomitantly with the exposed cohort for 25 years through December 31, 1996. Five control workers could not be followed up and were eliminated from the analysis. There were 42 deaths in this cohort, with 11 arising from lung cancer and none from mesothelioma.

Estimating Exposure Concentration

No regular measurements of airborne fiber concentration occurred in this plant, but respirable dust concentration was measured every 4 years. Results showed that conditions at the plant far exceeded the Chinese national standard of 2 mg/m^3. In June 1999, airborne dust and fiber concentrations were measured using personal samplers and the results were analyzed using PCM. Up to five workers in each section were monitored and measurements were performed in triplicate. The authors stated that they tried to choose the workers with the highest exposure level in each section of the plant. The results varied widely depending on the individual worker and the type of operation performed. The mean and ranges of values (taken from Table 1 of Yano et al. 2001) are summarized below:

Job Category	f/cc	mg/m^3
Opening raw material	6.5 (5.8 – 7.5)	8.8 (6.1 – 12.3)
Bagging raw material	12.6 (5.2 – 58.4)	18.2 (14.5 – 22.4)
Rubber plate	2.8 (2.6 – 3.1)	237.5 (176 – 320.5)
Textile	4.5 (0.7 – 17.0)	22.4 (15.8 – 35.5)
Asbestos cement	0.1	22.3

The authors noted that there was little apparent relation between dust levels and asbestos concentration.

Estimating Cumulative Exposure

Workers were grouped into seven major job categories as follows: office, asbestos cement, textile, maintenance, raw material, rear service, and rubber (friction) plate. For most of the workers, the jobs in which they were employed were relatively stable throughout the follow-up period. While no major job changes occurred, 20 men in the exposed cohort and 33 men in the control cohort left the plants before retirement.

Yano et al. (2001) did not report mortality as a function of cumulative exposure directly, but did report mortality and average duration of employment for three exposure categories, as follows (taken from Table 4 of Yano et al. 2001):

Exposure Category	Workplace Locations	Number of workers	Duration (yrs) Mean (Stdev)
Low	Office, asbestos cement	162	24.4 (6.8)
Intermediate	Maintenance, rear service, rubber plate	203	25.5 (8.1)
High	Raw material, textiles	150	23.5 (6.6)

Combining the information on exposure duration with the data on concentration by work area yields the following estimates of cumulative exposure for each exposure category:

Exposure Category	Workplace Locations	Mean Conc. (f/cc)	Mean Duration (yrs)	CE (f/cc-yr)
Low	Office, cement	0.1	24.4	2.44
Intermediate	Maintenance, rear service, rubber plate	2.8	25.5	71.4
High	Raw material, textiles	7.9 (a)	23.5	186

a) Average of 4.5, 6.5, and 12.6 f/cc

Smoking Data

Yano et al. (2001) reported that 77.1% of the asbestos workers smoked as compared to 50.4 % of the workers in the control cohort. Three workers in the exposed cohort and five workers in the control cohort quit smoking during the period of observation. The workers who smoked that were not exposed to asbestos did not have elevated lung cancer rates. According to the authors, the relative risk for smoking and lung cancer in China is between 2 and 4, which is lower than that found in Western countries (a relative risk of about 10 for all smokers).

Lung Cancer Results

Relative risk compared to the control cohort was calculated using the Cox proportional hazards model, adjusting for differences in age and smoking patterns. Based on this approach, the risk of lung cancer (not based on ICD coding) in the exposed cohort was 6.6-times that of the control cohort. When lung cancer risk was evaluated according to operation (exposure level), adjusted RR was highest for the raw material handling area (RR = 17.6), followed by the textile area (RR = 9.8), the maintenance section (RR = 7.3), and the cement/rubber plate area (RR = 2.5).

Because of the possibility of uncontrolled differences between the cohorts, the authors also performed a comparison within the exposed cohort, stratified into three exposure levels as described above. The lowest group was used as the reference. These results are shown in Figure A17-1. As seen, a clear dose-response increase in relative risk was observed. As described above, the cumulative exposure for each exposure group was based on multiplying the average duration as reported in Table 4 of Yano et al. (2001) by the average concentration as reported in Table 1 of Yano et al. (2001) for the corresponding job categories.

Mesothelioma Results

There were two reported cases of mesothelioma in the cohort, one pleural and the other peritoneal. Both of the cases were confirmed pathologically. These deaths constituted 1.5% of total mortality in the asbestos cohort. The man who developed pleural mesothelioma worked in the raw materials section of the plant and the man who developed the peritoneal mesothelioma worked in the textile section.

Table 2 of Yano et al. (2001) report the person years of observation for the cohort (11,525), the average exposure duration (24.6 years), and the average time since first exposure (33.8 years). The average concentration may be computed as the average of the concentrations (shown in Table 1 of Yano et al. 2001) and the number of people in each exposure category (shown in Table 4 of Yano et al. 2001). These data are shown in Figure A17-2.

Uncertainty Characterization

Appendix C discusses the primary sources of uncertainty in epidemiological studies of cancer risk from asbestos exposure in the workplace and describes the methods used in this document for characterizing the uncertainty. The following sections discuss the uncertainty characterization and issues of potential bias for this study.

Uncertainty Due to Measurement Error

As described in Section 3.1 of Appendix C, all estimates of concentration levels of asbestos in the workplace are uncertain due to the combination of sampling error and analytical error. These measurements are usually averaged according to job or work area, often stratified by time. For this study, Yano et al. (2001) report mean concentrations from measurements collected in 1999 as a function of job category (see Table 1 in the original report). The magnitude of the uncertainty in the reported mean value for each job/time category (which is used to compute cumulative exposure) is a function of a) the number of samples used to compute the mean, b) the between-sample variability, and c) the nature of the underlying distribution. As mentioned above, measurements were collected from as many as five workers in each plant section in triplicate. However, the authors do not provide information on the exact number of samples collected, or on the degree of between-sample variability. Therefore, in the absence of data, the default assumption described in Appendix C is applied to this study to account for measurement error, and is characterized as:

PDF(measurement error) ~ TRI(0.6, 1, 1.5)

Uncertainty in Mean Values for Exposure Groups

The cumulative exposure values for this cohort are estimated by multiplying reported average exposure durations by the average exposure concentration. Therefore, no uncertainty distributions are needed to account for using estimates of the mean.

Uncertainty in Conversion Factor (CF) from Dust Data (mppcf) to PCM f/cc

Airborne dust and fiber concentrations were measured using PCM analysis. Therefore, a conversion factor is not necessary for this cohort.

Uncertainty in the Use of Stationary Rather Than Personal Air Monitors

The survey conducted at the Chinese plant in June 1999 utilized personal air samplers to collect measurements of the work environment. Since personal monitors were used there is no uncertainty specified to account for the use of stationary monitors.

Uncertainty in Temporal Representativeness

Measurements reported for this cohort were only collected one on day in June 1999. The cohort was evaluated from January 1, 1972 to December 31, 1996. As described in Appendix C, when data are not representative of the exposure period of employees, the uncertainty associated with temporal representativeness is considered to be high, and is characterized as follows:

PDF(temporal representativeness) ~ TRI(0.5, 1, 1.5)

Bias for Use of CE Rather than CE10

This study reports cumulative exposure as CE rather than as CE10. As discussed in section 3.6 of Appendix C, use of CE rather than CE10 tends to bias results low, with the magnitude depending on the duration of exposure, the length of follow-up, and whether or not early person years of observation were excluded. Yano et al. (2001) report the average duration and follow-up as described above. The lung cancer mortality data based on the case-control study did not exclude any person-years of observation. Based on these study attributes a BCF for this cohort was determined to be:

BCF ~ TRI(1.3, 1.4, 1.5)

Uncertainty in Cumulative Exposure for Mesothelioma Analysis

This study reports two mesothelioma cases among the asbestos workers. The average value of cumulative exposure (C·Q) is estimated from the average duration (D) and average years of observation (T) reported in Table 2 (Yano et al. 2001), and an estimate of the average exposure concentration derived from a weighted average given the data in Tables 1 and 4 of Yano et al. (2001). As discussed in Section 3.7 of Appendix C, this approximation approach introduces uncertainty into the study-specific dose-response relationship, and this uncertainty may be approximated as follows:

PDF(approximation of C·Q) ~ TRI (0.75, 1, 1.4)

Uncertainty in Fraction Amphibole

As noted above, Yano et al. (2001) reported results of TEM and XRD analysis of four chrysotile samples used in the Chinese plant. The detection limit reported by the authors was 0.001%, and the authors found the samples to contain less than 0.001% amphibole. Even if trace levels were present, the level is sufficiently low that it is considered negligible for this analysis. Therefore, no uncertainty distribution is needed for fraction amphibole.

Uncertainty in Particle Size Data for Chrysotile

As mentioned above, the Chinese plant used only chrysotile asbestos. Of the TEM data sets available (see Appendix B), 11 are based on chrysotile asbestos. The Chinese plant encompasses a variety of industries including the manufacturing of cement products, textiles, and friction products. Of the 11 chrysotile data sets, three each correspond to the cement, textile, and friction product industries. Within an industry, the data sets differed by operation. There is no basis to select one data set over the other, so the nine chrysotile data sets were combined and applied to this study. The data sets match the epidemiology study for chrysotile asbestos and for each of the industries contained within the Chinese plant. Therefore, as described in Appendix C the uncertainty in f_{size} for chrysotile is low and is characterized as:

$$PDF(f_{size[chrysotile]}) \sim TRI(0.8, 1, 1.2)$$

Figure A17-1. Lung Cancer Data for Chinese Workers

Concentration (f/cc)		Duration	CE (PCM f/cc-yr)	Observed	Expected	Relative	Uncertainty Bounds	
Range (a)	Mean	(b)	Mean (c)	Deaths (b)	Deaths (d)	Risk (b)	5% LB	95% UB
0.1	0.1	24.4	2.44	2	2.0	1.00	0.29	2.77
2.6-3.1	2.8	25.5	71.4	7	1.9	3.60	1.87	6.43
4.5-12.6	7.9	23.5	186	13	1.6	8.10	5.03	12.50

a) Reported in Table 1 of Yano et al. (2001).
b) Reported in Table 4 of Yano et al. (2001).
c) Calculated as the average CE10 * Duration.
d) Calculated from the reported RR and number of observed deaths as Expected = Observed/RR.

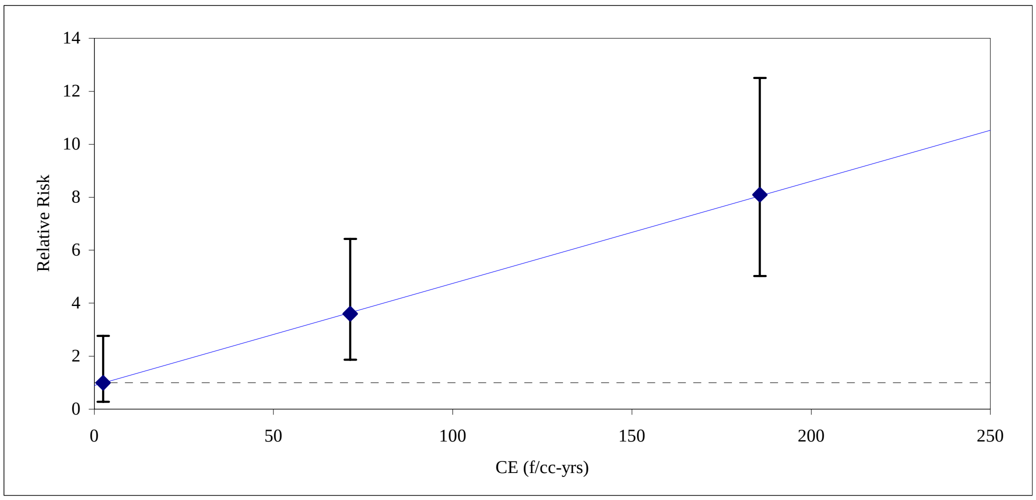
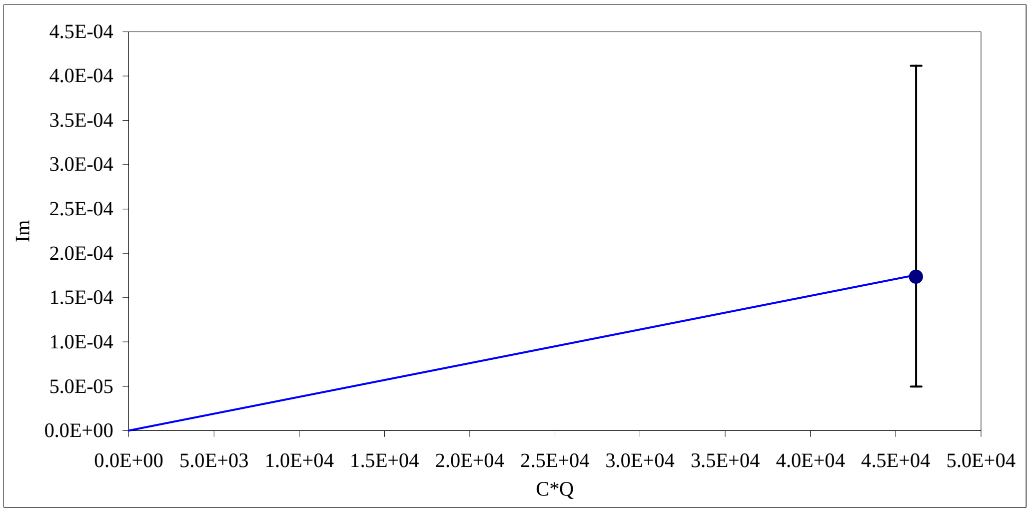


Figure A17-2. Mesothelioma Data for Chinese Workers

Yrs since 1st Exposure (a)	Duration (a)	Conc f/cc (b)	Q	Observed Deaths (a)	PY (a)	Incidence (Im)	Uncertainty Bounds	
							5% LB	95% UB
33.8	24.60	3.43	13481.27	2	11525	1.74E-04	5.0E-05	4.1E-04

(a) Reported in Table 2 (Yano et al. 2001)

(b) Calculated value based on weighted average given the number of workers in each job category reported in table 4, and the fiber concentrations by job category in table 1 (Yano et al. 2001).



APPENDIX A
ATTACHMENT 1

DATA REDUCTION METHOD FOR MESOTHELIOMA STUDIES REPORTED BY McDONALD ET AL. (1982, 1983, 1984)

1.0 INTRODUCTION

Parameterization of the absolute risk model for mesothelioma employed by USEPA requires data on the number of mesothelioma cases, the number of person-years of observation, and the cumulative exposure, which in turn requires data on the level of exposure, the exposure duration, and the time since first exposure. Three epidemiological reports by McDonald et al. (1982, 1983, 1984) provide data on the number of mesothelioma cases that were observed, but do not report the number of person years of observation, or the cumulative exposure. Nevertheless, it is possible to utilize information from the studies to estimate the data needed to utilize these three studies in the quantitative model fitting effort, as described below.

2.0 ESTIMATION OF PERSON-YEARS OF OBSERVATION

The number of person-years of observation is needed in order to compute the incidence of mesothelioma. In the case of the three studies by McDonald et al., the number of person years of observation may be estimated based on data that report the total number of deaths in the cohort, stratified by age at death. This section summarizes a procedure developed by Aeolus Inc. (2003) for performing this computation.

2.1 Basic Equations

Given the observed number of deaths (all cause) in an age group along with the Standardized Mortality Ratio (SMR) for the group, the expected number of deaths (all cause) in the group is computed as:

Expected Deaths (all cause) = Observed Deaths (all cause) / SMR

Given the expected number of all-cause deaths in some specified age bracket (a1 to a2), the total number of people N_{a1} who entered the age bracket alive may be computed as follows:

Let

p_i = probability of dying in year "i" from any cause, having entered year "i" alive

Then

$q_i = 1 - p_i$ = probability of surviving year "i" (all causes acting)

The probability of surviving a time window starting at age a1 and ending at age a2 is:

$$S_{a1,a2} = \prod_{i=a1}^{a2} q_i$$

Then

N_{a1} = (Expected Deaths)$_{a1,a2}$ / (1-$S_{a1,a2}$)

The number of person years of observation expected for a group of N_{a1} people between ages a1 and a2 is then computed as follows:

$$PY_{a1,a2} = N_{a1} \sum_{j=a1}^{a2} S_{a1,j}$$

2.2 Person-Year Reconstruction Calculations

Table 1 provides the all-cause mortality data reported in three published mesothelioma studies by McDonald et al. (1982, 1983, 1984). Using the data in this table, the number of person-years of observation is computed for each study as follows:

Step 1: Compute Expected Deaths

Age Bin	Pennsylvania (McDonald et al. 1982)			South Carolina (McDonald et al. 1983)			Connecticut (McDonald et al. 1984)		
	Observed Deaths	SMR	Expected Deaths	Observed Deaths	SMR	Expected Deaths	Observed Deaths	SMR	Expected Deaths
<45	191	1.09	175.2	178	1.274	139.7	139	1.085	128.1
45-64	667		611.9	502		394.0	616		567.7
≥65	534		489.9	177		138.9	511		471.0

Step 2: Compute Number of People Entering Each Age Bracket

This computation requires the all-cause mortality data for the reference population. Data for white males in the United States in 1971 are shown in Table 2. These data are used to compute the number of people entering each age bracket in each study as shown in Tables 3, 4, and 5. In each study, the lower bound of the youngest age bin was selected based on the reported average age at hire at each of the three asbestos plants studied by McDonald et al. (1982, 1983, 1984):

Mean Age at Hire (years)		
Pennsylvania	South Carolina	Connecticut
28.9 (29)	25.8 (26)	31.0 (31)

The upper bound of the upper age bin was set to 84 years in all cases. Based on these data, the probability of surviving from the start of an age bin to the end of an age bin is:

Pennsylvania	South Carolina	Connecticut
$S_{29\text{-}44} = 0.9550$	$S_{26\text{-}44} = 0.9440$	$S_{31\text{-}44} = 0.9525$
$S_{45\text{-}64} = 0.7352$	$S_{45\text{-}64} = 0.7352$	$S_{45\text{-}64} = 0.7352$
$S_{65\text{-}84} = 0.2155$	$S_{65\text{-}84} = 0.2155$	$S_{65\text{-}84} = 0.2155$

Hence, the number of people entering each age bracket is:

Pennsylvania	South Carolina	Connecticut
$N_{29} = 175.2/(1\text{-}0.9550) = 3{,}891$	$N_{26} = 139.7/(1\text{-}0.9440) = 2{,}494$	$N_{31} = 128.1/(1\text{-}0.9525) = 2{,}700$
$N_{45} = 611.9/(1\text{-}0.7352) = 2{,}311$	$N_{45} = 394.0/(1\text{-}0.7352) = 1{,}488$	$N_{45} = 567.7/(1\text{-}0.7352) = 2{,}144$
$N_{65} = 489.9/(1\text{-}0.2155) = 625$	$N_{65} = 138.9/(1\text{-}0.2155) = 177$	$N_{65} = 471.0/(1\text{-}0.2155) = 600$

Step 3: Compute Person-Years of Observation

From Tables 3 to 5,

Pennsylvania	South Carolina	Connecticut
$\sum_{j=29}^{44} S_{29,j} = 15.71$	$\sum_{j=26}^{44} S_{26,j} = 18.52$	$\sum_{j=31}^{44} S_{31,j} = 13.70$
$\sum_{j=45}^{64} S_{45,j} = 18.09$	$\sum_{j=45}^{64} S_{45,j} = 18.09$	$\sum_{j=45}^{64} S_{45,j} = 18.09$
$\sum_{j=65}^{84} S_{65,j} = 12.44$	$\sum_{j=65}^{84} S_{65,j} = 12.44$	$\sum_{j=65}^{84} S_{65,j} = 12.44$

Thus, the number of person-years of observation and the associated mesothelioma incidence associated with each age interval for each study is:

Pennsylvania	South Carolina	Connecticut
$PY_{29\text{-}44} = 3{,}891 \cdot 15.71 = 61{,}110$	$PY_{26\text{-}44} = 2{,}494 \cdot 18.52 = 46{,}173$	$PY_{31\text{-}44} = 2700 \cdot 13.70 = 36{,}978$
$PY_{45\text{-}64} = 2{,}311 \cdot 18.09 = 41{,}797$	$PY_{45\text{-}64} = 1{,}488 \cdot 18.09 = 26{,}914$	$PY_{45\text{-}64} = 2{,}144 \cdot 18.09 = 38{,}779$
$PY_{65\text{-}85} = 625 \cdot 12.44 = 7{,}767$	$PY_{65\text{-}85} = 177 \cdot 12.44 = 2{,}203$	$PY_{65\text{-}85} = 600 \cdot 12.44 = 7{,}466$
Total PY = 110,673	Total PY = 75,289	Total PY = 83,223

3.0 ESTIMATION OF CUMULATIVE EXPOSURE

None of the mesothelioma studies published by McDonald et al. include cumulative exposure data suitable for inclusion in the quantitative risk model. However, the cumulative exposure can be estimated for each exposure group as follows.

Step 1: Estimate Average Value of T

The average value of T (time since first exposure) may be estimated as:

$$\overline{T} = \text{(Average age at observation)} - \text{(average age at first employment)}$$

The value of average age at observation is based on the mid-point of the age strata used to report all-cause mortality and used to compute person-years of observation:

Reference/Cohort	Age Stratum	Average Age at First Exposure	Average Age at Observation	Average T
McDonald et al. 1982 Pennsylvania	<45	28.92	36.5 (a)	7.5
	45-64		54.5 (b)	25.6
	≥65		75 (b)	46.1
McDonald et al. 1983 South Carolina	<45	25.77	34.9 (a)	9.1
	45-64		54.5 (b)	28.7
	≥65		75 (b)	49.2
McDonald et al. 1984 Connecticut	<45	30.95	37.5 (a)	6.5
	45-64		54.5 (b)	23.6
	≥65		75 (b)	44.1

(a) Computed as the midpoint between the average age at first exposure and 44

(b) Computed as the midpoint of the age bin

Step 2: Compute Average Value of Q

Recall that the value of Q is given by:

$$
\begin{array}{ll}
Q = 0 & T < 10 \\
Q = (T-10)^3 & 10 < T \leq d + 10 \\
Q = (T-10)^3 - (T - 10 - d)^3 & T > d + 10
\end{array}
$$

The average value of d is reported in each paper by McDonald et al., which can be used to compute the average value of Q as follows:

Cohort	Age Stratum	Average Exposure Duration (d)	Average Time Since First Exposure (T)	Average Q
Pennsylvania	<45	9.18	7.5	0
	45-64		25.6	3,520
	≥65		46.1	27,503
South Carolina	<45	7.59	9.1	0
	45-64		28.7	5188
	≥65		49.2	28,700
Connecticut	<45	8.04	6.5	0
	45-64		23.6	2,321
	≥65		44.1	21,881

Step 3: Compute Bin-Specific Average Values of C·Q

The value off C·Q is simply the product of Q (calculated above) and the average value of C:

Cohort	Age Stratum	Average Exposure Concentration (C) (f/cc)	Average value of Q	Average value of C·Q
Pennsylvania	<45	6.96	0.0E+00	0.0E+00
	45-64		3.5E+03	2.5E+04
	≥65		2.8E+04	1.9E+05
South Carolina	<45	10.80	0.0E+00	0.0E+00
	45-64		5.2E+03	5.6E+04
	≥65		2.9E+04	3.1E+05
Connecticut	<45	5.52	0.0E+00	0.0E+00
	45-64		2.3E+03	1.3E+04
	≥65		2.2E+04	1.2E+05

Step 4: Compute Cohort-Wide Average Value of C:Q

Because the age at which the mesothelioma deaths occurred is not reported for the study by McDonald et al. (1982), it is not possible to stratify the mesothelioma cases according to age group. Therefore, the data for this study (and both other McDonald studies) were combined into one group by computing the person-year weighted average value of C·Q:

Cohort	Age Stratum	PY of Observation	Average value of C·Q	PY-Weighted Average value of C·Q
Pennsylvania	<45	61,110	0.0E+00	2.3E+04
	45-64	41,797	2.5E+04	
	≥65	7,767	1.9E+05	
South Carolina	<45	46,173	0.0E+00	2.9E+04
	45-64	26,914	5.6E+04	
	≥65	2,203	3.1E+05	
Connecticut	<45	36,978	0.0E+00	1.7E+04
	45-64	38,779	1.3E+04	
	≥65	7,466	1.2E+05	

It should be noted that combining data into one group does not result in a loss of information, since the MLE slope of the exposure-response line (the study-specific KM) is the same whether data are combined or kept separated.

4.0 DATA SUMMARY

Based on the methods described above, data for each of the three studies that may be used in the quantitative model fitting exercise are as follows:

Parameter	Pennsylvania	South Carolina	Connecticut
Mesothelioma Cases	14	1	0
Est. Total PY of Observation	110,673	75,289	83,223
Est. mean C·Q	2.3E+04	2.9E+04	1.7E+04

5.0 REFERENCES

Aeolus. 2003. Technical Support Document for a Protocol to Assess Asbestos-Related Risk. Report 9345.4-06, prepared for U.S. Environmental Protection Agency, Office of Solid Waste and Emergency Response by Berman DW (Aeolus Inc.) and Crump K (Environ Corp).

DHHS. 1971. Vital Statistics of the United States 1971, Volume 2, Section 5 – Life Tables. U.S. Department of Health, Education, and Welfare, Public Heath Service, Health Resources Administration, National Center for Health Statistics.

McDonald AD, Fry JS, Woolley AJ, McDonald JC. 1982. Dust Exposure and Mortality in an American Factory Using Chrysotile, Amosite, and Crocidolite in Mainly Textile Manufacture. British Journal of Industrial Medicine 39:368–374.

McDonald AD, Fry JS, Wooley AJ, McDonald JC. 1983. Dust Exposure and Mortality in an American Chrysotile Textile Plant. British Journal of Industrial Medicine. 39:361–367.

McDonald AD, Fry JS, Woolley AJ, McDonald JC. 1984. Dust Exposure and Mortality in an American Chrysotile Asbestos Friction Products Plant. British Journal of Industrial Medicine. 41:151–157.

TABLE 1 ALL-CAUSE MORTALITY DATA REPORTED IN McDONALD ET AL. (1982, 1983, 1984)

Age Range	Deaths (All cause)			SMR (All cause)		
	Pennsylvania	South Carolina	Connecticut	Pennsylvania	South Carolina	Connecticut
< 45	191	178	139			
45-64	667	502	616			
≥ 65	534	177	511			
Total	1,392	857	1,392	1.09	1.274	1.085

TABLE 2 MORTALITY STATISTICS FOR WHITE MALES (1971)

Age Interval	Probability of Death (p)	
	Within the age interval	Average probability for each year[a]
0 - 1	0.0191	0.01910
1 - 5	0.0032	0.00080
5 - 10	0.0022	0.00044
10 - 15	0.0024	0.00048
15 - 20	0.0074	0.00148
20 - 25	0.0095	0.00191
25 - 30	0.0082	0.00165
30 - 35	0.0090	0.00181
35 - 40	0.0127	0.00255
40 - 45	0.0202	0.00407
45 - 50	0.0325	0.00659
50 - 55	0.0523	0.01069
55 - 60	0.0826	0.01709
60 - 65	0.1260	0.02658
65 - 70	0.1785	0.03856
70 - 75	0.2559	0.05740
75 - 80	0.3582	0.08488
80 - 85	0.4507	0.11292
> 85	1	

Source: DHHS (1971). Date are for white males (Table 5-1)

[a] For an age interval of n years, calculated as $1-(1-p)^{(1/n)}$

TABLE 3 PERSON-YEAR CALCULATIONS FOR THE PENNSYLVANIA COHORT (McDONALD ET AL. 1982)

Age 29-44

Age (i)	p(i)	q(i)	S(20,j)
29	0.00385	0.99615	1.00000
30	0.00181	0.99819	0.99615
31	0.00181	0.99819	0.99435
32	0.00181	0.99819	0.99255
33	0.00181	0.99819	0.99076
34	0.00181	0.99819	0.98897
35	0.00255	0.99745	0.98719
36	0.00255	0.99745	0.98466
37	0.00255	0.99745	0.98215
38	0.00255	0.99745	0.97964
39	0.00255	0.99745	0.97714
40	0.00407	0.99593	0.97465
41	0.00407	0.99593	0.97068
42	0.00407	0.99593	0.96672
43	0.00407	0.99593	0.96279
44	0.00407	0.99593	0.95887

S(29-44) = 0.9550

Σ S(20,j) = 15.71

Age 45-64

Age (i)	p(i)	q(i)	S(45,j)
45	0.00659	0.99341	1.00000
46	0.00659	0.99341	0.99341
47	0.00659	0.99341	0.98687
48	0.00659	0.99341	0.98037
49	0.00659	0.99341	0.97391
50	0.01069	0.98931	0.96750
51	0.01069	0.98931	0.95716
52	0.01069	0.98931	0.94693
53	0.01069	0.98931	0.93681
54	0.01069	0.98931	0.92680
55	0.01709	0.98291	0.91690
56	0.01709	0.98291	0.90123
57	0.01709	0.98291	0.88582
58	0.01709	0.98291	0.87068
59	0.01709	0.98291	0.85579
60	0.02658	0.97342	0.84116
61	0.02658	0.97342	0.81881
62	0.02658	0.97342	0.79705
63	0.02658	0.97342	0.77587
64	0.02658	0.97342	0.75525

S(45-64) = 0.7352

Σ S(45,j) = 18.09

Age 65-84

Age (i)	p(i)	q(i)	S(65,j)
65	0.03856	0.96144	1.00000
66	0.03856	0.96144	0.96144
67	0.03856	0.96144	0.92436
68	0.03856	0.96144	0.88872
69	0.03856	0.96144	0.85445
70	0.05740	0.94260	0.82150
71	0.05740	0.94260	0.77434
72	0.05740	0.94260	0.72989
73	0.05740	0.94260	0.68800
74	0.05740	0.94260	0.64850
75	0.08488	0.91512	0.61128
76	0.08488	0.91512	0.55940
77	0.08488	0.91512	0.51192
78	0.08488	0.91512	0.46847
79	0.08488	0.91512	0.42871
80	0.11292	0.88708	0.39232
81	0.11292	0.88708	0.34802
82	0.11292	0.88708	0.30872
83	0.11292	0.88708	0.27386
84	0.11292	0.88708	0.24293

S(65-84) = 0.2155

Σ S(65,j) = 12.44

p(i) = probability of dying in year i, conditional on entering year i alive

q(i) = probability of surviving year i

S(i,j) = probability of entering year j alive, conditional on being alive at the start of year i

PY RECONSTRUCTION

Age Group	N Dead	SMR	Expected	S(a,b)	N Entering	ΣS(a,b)	PY
20-44	191	1.09	175.2	0.9550	3890.5	15.71	61,110
45-64	667	1.09	611.9	0.7352	2310.7	18.09	41,797
65-84	534	1.09	489.9	0.2155	624.5	12.44	7,767
Total	1392						110,673

TABLE 4 PERSON-YEAR CALCULATIONS FOR THE SOUTH CAROLINA COHORT (McDONALD ET AL. 1983)

Age 26-44

Age (i)	p(i)	q(i)	S(20,j)
26	0.00385	0.99615	1.00000
27	0.00385	0.99615	0.99615
28	0.00385	0.99615	0.99232
29	0.00385	0.99615	0.98850
30	0.00181	0.99819	0.98469
31	0.00181	0.99819	0.98291
32	0.00181	0.99819	0.98114
33	0.00181	0.99819	0.97936
34	0.00181	0.99819	0.97759
35	0.00255	0.99745	0.97583
36	0.00255	0.99745	0.97334
37	0.00255	0.99745	0.97085
38	0.00255	0.99745	0.96837
39	0.00255	0.99745	0.96590
40	0.00407	0.99593	0.96344
41	0.00407	0.99593	0.95951
42	0.00407	0.99593	0.95560
43	0.00407	0.99593	0.95171
44	0.00407	0.99593	0.94783

S(26-44) = 0.9440

Σ S(20,,j) = 18.52

Age 45-64

Age (i)	p(i)	q(i)	S(45,j)
45	0.00659	0.99341	1.00000
46	0.00659	0.99341	0.99341
47	0.00659	0.99341	0.98687
48	0.00659	0.99341	0.98037
49	0.00659	0.99341	0.97391
50	0.01069	0.98931	0.96750
51	0.01069	0.98931	0.95716
52	0.01069	0.98931	0.94693
53	0.01069	0.98931	0.93681
54	0.01069	0.98931	0.92680
55	0.01709	0.98291	0.91690
56	0.01709	0.98291	0.90123
57	0.01709	0.98291	0.88582
58	0.01709	0.98291	0.87068
59	0.01709	0.98291	0.85579
60	0.02658	0.97342	0.84116
61	0.02658	0.97342	0.81881
62	0.02658	0.97342	0.79705
63	0.02658	0.97342	0.77587
64	0.02658	0.97342	0.75525

S(45-64) = 0.7352

Σ S(45,,j) = 18.09

Age 65-84

Age (i)	p(i)	q(i)	S(65,j)
65	0.03856	0.96144	1.00000
66	0.03856	0.96144	0.96144
67	0.03856	0.96144	0.92436
68	0.03856	0.96144	0.88872
69	0.03856	0.96144	0.85445
70	0.05740	0.94260	0.82150
71	0.05740	0.94260	0.77434
72	0.05740	0.94260	0.72989
73	0.05740	0.94260	0.68800
74	0.05740	0.94260	0.64850
75	0.08488	0.91512	0.61128
76	0.08488	0.91512	0.55940
77	0.08488	0.91512	0.51192
78	0.08488	0.91512	0.46847
79	0.08488	0.91512	0.42871
80	0.11292	0.88708	0.39232
81	0.11292	0.88708	0.34802
82	0.11292	0.88708	0.30872
83	0.11292	0.88708	0.27386
84	0.11292	0.88708	0.24293

S(65-84) = 0.2155

Σ S(65,,j) = 12.44

p(i) = probability of dying in year i, conditional on entering year i alive

q(i) = probability of surviving year i

S(i,j) = probability of entering year j alive, conditional on being alive at the start of year i

PY RECONSTRUCTION

Age Group	N Dead	SMR	Expected	S(a,b)	N Entering	ΣS(a,b)	PY
20-44	178	1.274	139.7	0.9440	2493.8	18.52	46,173
45-64	502	1.274	394.0	0.7352	1487.9	18.09	26,914
65-84	177	1.274	138.9	0.2155	177.1	12.44	2,203
Total	857						75,289

TABLE 5 PERSON-YEAR CALCULATIONS FOR THE CONNECTICUT COHORT (McDONALD ET AL. 1984)

Age 31-44

Age (i)	p(i)	q(i)	S(20,j)
31	0.00385	0.99615	1.00000
32	0.00385	0.99615	0.99615
33	0.00385	0.99615	0.99232
34	0.00385	0.99615	0.98850
35	0.00255	0.99745	0.98469
36	0.00255	0.99745	0.98218
37	0.00255	0.99745	0.97967
38	0.00255	0.99745	0.97717
39	0.00255	0.99745	0.97467
40	0.00407	0.99593	0.97219
41	0.00407	0.99593	0.96823
42	0.00407	0.99593	0.96428
43	0.00407	0.99593	0.96035
44	0.00407	0.99593	0.95644

S(31-44) = 0.9525

Σ S(20,j) = 13.70

Age 45-64

Age (i)	p(i)	q(i)	S(45,j)
45	0.00659	0.99341	1.00000
46	0.00659	0.99341	0.99341
47	0.00659	0.99341	0.98687
48	0.00659	0.99341	0.98037
49	0.00659	0.99341	0.97391
50	0.01069	0.98931	0.96750
51	0.01069	0.98931	0.95716
52	0.01069	0.98931	0.94693
53	0.01069	0.98931	0.93681
54	0.01069	0.98931	0.92680
55	0.01709	0.98291	0.91690
56	0.01709	0.98291	0.90123
57	0.01709	0.98291	0.88582
58	0.01709	0.98291	0.87068
59	0.01709	0.98291	0.85579
60	0.02658	0.97342	0.84116
61	0.02658	0.97342	0.81881
62	0.02658	0.97342	0.79705
63	0.02658	0.97342	0.77587
64	0.02658	0.97342	0.75525

S(45-64) = 0.7352

Σ S(45,j) = 18.09

Age 65-84

Age (i)	p(i)	q(i)	S(65,j)
65	0.03856	0.96144	1.00000
66	0.03856	0.96144	0.96144
67	0.03856	0.96144	0.92436
68	0.03856	0.96144	0.88872
69	0.03856	0.96144	0.85445
70	0.05740	0.94260	0.82150
71	0.05740	0.94260	0.77434
72	0.05740	0.94260	0.72989
73	0.05740	0.94260	0.68800
74	0.05740	0.94260	0.64850
75	0.08488	0.91512	0.61128
76	0.08488	0.91512	0.55940
77	0.08488	0.91512	0.51192
78	0.08488	0.91512	0.46847
79	0.08488	0.91512	0.42871
80	0.11292	0.88708	0.39232
81	0.11292	0.88708	0.34802
82	0.11292	0.88708	0.30872
83	0.11292	0.88708	0.27386
84	0.11292	0.88708	0.24293

S(65-84) = 0.2155

Σ S(65,j) = 12.44

p(i) = probability of dying in year i, conditional on entering year i alive

q(i) = probability of surviving year i

S(i,j) = probability of entering year j alive, conditional on being alive at the start of year i

PY RECONSTRUCTION

Age Group	N Dead	SMR	Expected	S(a,b)	N Entering	ΣS(a,b)	PY
30-44	139	1.085	128.1	0.9525	2699.7	13.70	36,978
45-64	616	1.085	567.7	0.7352	2143.9	18.09	38,779
65-84	511	1.085	471.0	0.2155	600.3	12.44	7,466
Total	1266						83,223