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ESTIMATES OF DOSE–RESPONSE FOR RESPIRATORY CANCER AMONG CHRYSOTILE ASBESTOS TEXTILE WORKERS

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Abstract—Methods for reconstructing historic dust exposures, taking into account jobs and controls, were developed and combined with a retrospective cohort mortality study of chrysotile asbestos textile workers, between 1940 and 1975, to evaluate dose–response relationships for lung cancer and nonmalignant respiratory diseases. Among 768 white males, statistically significant excess mortality was observed for lung cancer (SMR = 348) and nonmalignant respiratory diseases (SMR = 263). There were 15 deaths due to asbestosis or pulmonary fibrosis. Using estimated fibre dose by job and calendar time, combined with detailed work histories, mortality by cumulative dose was investigated. For lung cancer, a linear dose–response relationship was obtained with an SMR of 223 in the lowest cumulative dose category. Significant dose–response relationships were also observed for nonmalignant respiratory diseases excluding acute upper respiratory infection, influenza, pneumonia and bronchitis. Of the 191 deaths among white males, only one was due to mesothelioma.

INTRODUCTION

IT IS well established that occupational exposure to asbestos is associated with increased risks of many diseases including pulmonary fibrosis (asbestosis), respiratory cancer, mesothelioma of both pleural and peritoneal tissues and cancer of the gastrointestinal tract. These health effects have been shown repeatedly using different populations and study methods (NIOSH, 1976; IARC, 1977).

Although there has been a large amount of research devoted to asbestos, there have been few epidemiological studies of cancer risks among workers exposed only to chrysotile, which accounts for more than 90% of all asbestos used in the U.S.A. Even fewer studies have attempted to develop exposure estimates and to investigate dose–response relationships in a quantitative manner.

To provide further information on lung cancer risks associated with chrysotile exposures, a retrospective mortality study was conducted among a cohort of asbestos textile workers. The mortality data were combined with fibre exposure estimates to investigate dose–response relationships for lung cancer and nonmalignant respiratory diseases.

The plant selected for study is unique in several ways. First, only an insignificant quantity of asbestos fibre other than chrysotile was ever processed. Secondly, the plant was engaged in a progressive dust control programme beginning in the mid-1930s; therefore, the possibility of evaluating effects at exposure levels lower than those of previous studies existed. Perhaps more important is the fact that a considerable quantity of exposure data was available for estimation of worker exposures.

METHODS

Cohort mortality study

Although the plant under study began production of asbestos products in 1896, detailed personnel records were first maintained beginning in approximately 1930. The record system has remained remarkably unchanged since that time. For each worker, an employment card was completed at initial employment giving name, date of birth, sex, race, social security number, marital status and address. This same card also contained the detailed work history giving exact dates of employment by plant department and specific job. All information from these cards was entered onto a computer data file.

The cohort was limited to 768 white males employed six or more months in textile production operations with at least one month of employment between 1 January 1940 and 31 December 1965. The cohort was followed through 31 December 1975. The 1965 cut-off date for cohort entry was chosen to insure that all workers would have a minimum "latency" of 10 yr by the study end date.

An attempt was made to determine the vital status of all cohort members on 31 December 1975. The primary sources of information used for this follow-up included the Social Security Administration (SSA), Internal Revenue Service (IRS), U.S. Postal Mail Correction Service, state drivers licence files and state vital statistics offices. Individuals not located through these primary sources were traced using local records such as telephone listings, Polk directories, property records, voter records, records of funeral homes and various other local sources.

Cause specific standardized mortality ratios (SMRs) were calculated using a life table analysis based on the technique developed by CUTLER and EDERER (1958). Person-years at risk of dying were distributed by 5 yr age, calendar time and time since initial employment (latency) groups. Person-years were accumulated for each cohort member beginning when all requirements for cohort entry were met until the date of death or 31 December 1975. Those whose vital status remained unknown were assumed alive at the study cut-off date, thereby contributing their maximum possible person-years to the analysis.

The follow-up period for this study spans the Fifth–Eighth Revisions of the International Lists of Diseases and Causes of Death. Death certificates were coded by a qualified nosologist according to the ICDA revision in effect at the time of death. All death codes were then grouped into 89 death categories based on the Seventh Revision for purposes of standardization. Individuals known to be deceased, but for whom no death certificates were available, were assumed to be deceased, cause unknown.

The numbers of expected deaths, standardized for sex, age, race and calendar time, were calculated by application of cause specific death rates for the total U.S.A. to the person-years at risk of dying. Death rates specific to the 89 Seventh Revision death groups were calculated from yearly tallies of deaths and census data.

For evaluating dose–response, cumulative exposure strata were created and a worker was moved from one stratum to the next as his cumulative exposure increased during the course of follow-up (BRESLOW, 1976; LUNDIN *et al.*, 1971). By this method, a worker contributed person-years and thus expected deaths in several exposure strata while contributing observed death to only the highest stratum achieved. Each worker's cumulative exposure was estimated by combining detailed work histories from plant employment records with estimates of exposure by job.

Statistical significance of observed cause specific excesses or deficits was evaluated using the Poisson distribution (PEARSON and HARTLEY, 1958).

Exposure estimates

From 1930 to 1975, 5952 environmental samples were collected in the plant under study as shown in Table 1. Prior to 1965, all samples were of the impinger type; from 1965 until 1971 membrane filter samples were also collected. In 1971, the impinger method was entirely replaced by the membrane filter method.

TABLE 1. SUMMARY OF SOURCES OF INDUSTRIAL HYGIENE SAMPLING DATA FOR 1930–1975

Source of sample data	Number of samples 1930–1945	1945–1960	1960–1975
Company sampling program		179	4919
Company insurance carrier	112		
State Board of Health	12	4	
U.S. Public Health Service	69		657
Total number of samples	193	183	5576

For purposes of estimating worker exposure levels, it was necessary that all exposure data be of the same unit of measure; therefore, a conversion from impinger counts, measured in millions of particles per cubic foot of air (MPPCF), to membrane filter counts, measured as fibres longer than 5 μm per cubic centimetre of air (fibres cm^{-3}) was necessary. Fortunately, there were two relatively good sources of data for this estimate; 120 paired impinger–membrane filter samples collected in this plant by the U.S. Public Health Service in 1965 and 986 concurrent samples by these two methods in plant operations collected during 1968–1971. Relationships between the two methods were investigated using multiple linear regression. Results of these conversion estimates and approx. 95% confidence intervals are given in Fig. 1. For all textile operations except preparation a conversion of 3 fibre cm^{-3} for 1 MPPCF was

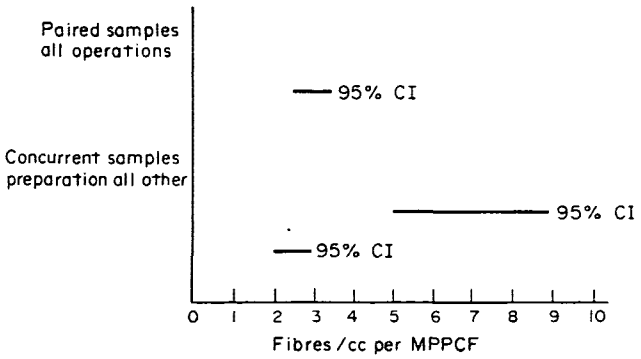

FIG. 1. Comparison of mean impinger–membrane filter conversions obtained for paired sample and concurrent sample analyses.

used. For preparation, a conversion of 8 fibre cm^{-3} was used. Using these conversion values, all sample data were expressed as fibres cm^{-3}.

Mean exposure levels by job between 1930 and 1975 were estimated using linear statistical models. Textile operations were divided into 16 exposure zones according to similarity of processes and exposures as described by CORN and ESMEN (1979). All jobs within each exposure zone were further assigned to one of four Uniform Job Categories (UJC) based upon tasks associated with the particular job (ESMEN, 1979).

Using the exposure zone and Uniform Job Categories, linear models were developed to allow estimation of worker exposures in each exposure zone over time; taking into account changes in processes and engineering controls. The linear model for each exposure zone took the following form:

$$\bar{y}_i = \sum_k \beta_{ik} Z_{ik} + \sum_j \alpha_{ij} Z_{ij} + \sum_t \delta_{it} Z_{it},$$

where:

$\bar{y}_i$ = mean of log of concentration values for exposure zone i,
β_{ik} = multiple regression parameter for UJC k in exposure zone i,
Z_{ik} = independent variable used to identify UJC k in exposure zone i,
δ_{ij} = multiple regression parameter for control j in exposure zone i,
Z_{ij} = independent variable used to represent dates of control changes for exposure zone i,
δ_{it} = multiple regression parameter for time interval t in exposure zone i,
Z_{it} = independent variable used to represent calendar time periods
$E = N(0, \sigma^2)$

The first term in the model for each exposure zone takes into account Uniform Job Category, the second term accounts for process or control changes and the third term is used to account for any residual time trends in the data. Details regarding process and control changes were determined through studies of plant engineering records and reports, discussions with long-term employees and from data collected by the U.S. Public Health Service.

Parameters of the exposure models were estimated by multiple linear regression using the historic industrial hygiene data. The regression models predict the mean for the log of dust concentration values; however, others have shown that the arithmetic mean may give the best estimation of the average concentration to which workers are exposed (SHERWOOD, 1966; COENEN, 1966; COENEN, 1971; LEIDEL and BUSCH, 1975). This is especially true when short "grab" samples of approximately equal sampling duration are used to estimate worker exposures, as in the present study. Mean exposures were estimated by the following expression:

$$\bar{x} = \exp(\bar{y} + \tfrac{1}{2}\sigma^2),$$

where:

$\bar{x}$ = estimated arithmetic mean concentration,
$\bar{y}$ = mean of log concentration values
and σ^2 = pooled estimate of variance of y from the regression model.

Details of all methods used in this study have been presented elsewhere (DEMENT, 1980).

RESULTS

Mortality study

Results of the follow-up efforts are summarized in Table 2. Vital status was determined for 97.1% of the cohort. Of the 191 deaths, all but 13 death certificates were obtained.

A total of 21 158 person-years at risk were experienced by white males between 1 January 1940, and 31 December 1975. Observed and expected deaths by cause are given in Table 3.

Among white males, 191 deaths were observed, whereas only 141.84 were expected (SMR = 135, $p < 0.01$). Other disease categories showing significant excesses were all malignant neoplasms (SMR = 174, $p < 0.01$) and nonmalignant respiratory diseases (SMR = 263, $p < 0.01$).

TABLE 2. SUMMARY OF COHORT DEMOGRAPHIC DATA AND VITAL STATUS AS OF 31 DECEMBER 1975, WHITE MALES

Vital status	Number	(%)
Known to be alive	555	
Known to be deceased	191	
Death certificate obtained	178	(93.19)
Death certificate not obtained	13	(6.81)
Unknown vital status	22	(2.86)
Total	768	

TABLE 3. OBSERVED AND EXPECTED DEATHS BY CAUSE FOR WHITE MALE ASBESTOS TEXTILE WORKERS, 1940–1975

Cause of death	ICDA 7th List No.	Obs.	Exp.	SMR
All causes		191	141.84	135†
Malignant neoplasms		43	24.66	174†
Digestive system	150–159	9	7.10	127
Trachea, bronchus & lung	162–163	26	7.47	348†
Other & unspecified sites		8	10.09	79
Disease of the central nervous system	330–334, 345	9	7.72	117
Disease of the circulatory system	400–468	58	57.43	101
All tuberculosis	001–019	4	2.77	144
Nonmalignant respiratory disease		18	6.85	263†
Acute upper respiratory infection	470–475	0	0.04	—
Influenza	480–483	0	0.37	—
Pneumonia	490–493	0	2.98	—*
Bronchitis	500–502	0	0.41	—
Other respiratory diseases	510–527	18	3.05	590†
Accidents	800–962	14	16.64	84
Other violent deaths	963–964, 970–985	7	6.10	115
All other known causes		23	17.92	128
Unknown causes		15	1.75	—

*$p < 0.05$.
†$p < 0.01$.

Table 3 shows the elevated SMR for all malignant neoplasms among whites to be largely accounted for by cancer of the trachea, bronchus and lung. A total of 26 lung cancers were observed and only 7.47 were expected (SMR = 348, $p < 0.01$). Table 4 shows observed and expected lung cancer deaths by interval since initial employment (latency). Of the 26 deaths due to lung cancer, 15 occurred after 30 or more years latency. The SMR for lung cancer demonstrated an increasing trend with latency reaching 444 at greater than 30 yr.

TABLE 4. OBSERVED AND EXPECTED DEATHS DUE TO LUNG CANCER (ICDA 162, 163) BY TIME INTERVAL SINCE INITIAL EMPLOYMENT AND DURATION OF EMPLOYMENT, WHITE MALES

Years since initial employment	Obs.	Deaths exp.	SMR
< 10	0	0.37	
10–19	3	1.40	214
20–29	8	3.00	267†
≥ 30	15	2.70	444†
Years employed	**Obs.**	**Deaths exp.**	**SMR**
< 10	9	4.98	181
10–19	4	1.00	400*
20–29	12	1.00	1200*
≥ 30	1	0.47	213
Total	26	7.47	348*

*$p < 0.05$.
†$p < 0.10$.

Using duration of employment as a surrogate for cumulative fibre dose, dose-response relationships for lung cancer are given in Table 4. These data demonstrate an increasing trend in the lung cancer SMR with duration of employment.

All 18 of the nonmalignant respiratory disease deaths fell into the category "other respiratory diseases" excluding upper respiratory infection, influenza, pneumonia and bronchitis. Of these 18 deaths, asbestosis or pulmonary fibrosis was the underlying cause of death for 15, one was due to emphysema, one septicemia and one pulmonary edema. Other significant conditions mentioned on the death certificates of the 15 asbestosis deaths include bronchitis on two certificates and chronic obstructive lung disease on one certificate.

The SMR for other nonmalignant respiratory diseases also demonstrated no trend with latency but some increasing trends with employment duration (Table 5). Nine of the 18 deaths occurred after 30 or more years since initial employment (SMR = 763, $p < 0.01$).

Only one mesothelioma was observed among white males. This was a peritoneal mesothelioma confirmed by autopsy. The interval (latency) between initial employment and death was 34 yr. There were several other deaths which mentioned 'cancer of

TABLE 5. OBSERVED AND EXPECTED DEATHS DUE TO 'OTHER NONMALIGNANT RESPIRATORY DISEASES' BY TIME INTERVAL SINCE INITIAL EMPLOYMENT AND DURATION OF EMPLOYMENT, WHITE MALES

Years since initial employment	Obs.	Deaths exp.	SMR
<10	1	0.21	
10–19	4	0.51	784†
20–29	4	1.14	350*
≥30	9	1.18	763†
Years employed	**Obs.**	**Deaths exp.**	**SMR**
<10	3	1.99	157
10–19	6	0.39	1538†
20–29	7	0.42	1667†
≥30	2	0.22	895
Total	18	3.05	590

*$p < 0.05$.
†$p < 0.01$.

the abdomen' which may be suspect; however, no autopsy or other confirmatory data were available.

Digestive system cancers were only slightly elevated in this cohort. In addition to the peritoneal mesothelioma mentioned above, other digestive system cancers included one esophageal, two stomach, one intestinal, two liver, and two pancreatic cancers; however, none of these sites were statistically elevated.

Exposures and dose–response

Estimated mean exposures by Uniform Job Category and time period are summarized in Table 6. Before 1940, mean exposures as high as 78.0 fibres cm^{-3} were estimated for certain dusty jobs in the preparation department. After 1940, mean exposures generally were between 5 and 10 fibres cm^{-3} except for persons handling raw fibre.

Both lung cancer and asbestosis require lengthy periods from initial exposure to become clinically evident. In the present study, no asbestosis or lung cancer deaths occurred among white males prior to 15 yr after initial employment (latency). For dose–response studies, it is important to restrict the analyses to those achieving sufficient latency to be 'at risk' of dying from lung cancer or asbestosis. For this reason, the present dose-response analyses were restricted to those achieving 15 or more years since initial employment (latency). This was accomplished by beginning accumulation of person-years for each worker after the 15 yr latency period was satisfied. Those dying before reaching 15 yr latency were excluded.

Results of the dose–response analyses for all causes, diseases of the circulatory system, lung cancer, and other nonmalignant respiratory diseases are given in Table 7. The SMR for all causes was elevated for all exposure categories increasing to 235 in the

TABLE 6. SUMMARY OF ESTIMATED MEAN FIBRE EXPOSURES BY OPERATION, CALENDAR TIME AND UNIFORM JOB CATEGORIES

Plant operation and calendar time period	Estimated mean exposure by UJC (fibres >5 μm cm^{-3}) A General area	B, Machine operators Sub-category 1	Sub-category 2	Sub-category 3	Sub-category 4	C Clean-up	D Raw fibre handling
Preparation/waste recovery							
1930–1944	26.2	78.0	78.0	45.9		54.4	35.0
1945–1964	8.1	23.9	23.9	14.1		16.7	10.8
1965–1975	5.8	17.2		10.1		12.0	7.3
Carding							
1930–1935	10.8	13.3				18.1	22.8
1936–1945	5.3	6.5				8.8	11.0
1946–1965	2.4	2.9				4.0	5.0
1966–1975	4.3	5.3				7.2	9.0
Ring spinning							
1930–1965	8.2	6.6				N	N
1966–1970	8.6	6.9				N	N
1971–1975	6.2	5.0				N	N
Mule spinning							
1930–1975	4.6	4.6				6.7	N
Foster winding							
1930–1937	10.4	13.6				20.9	N
1938–1975	4.2	5.5				8.4	N
Twisting							
1930–1938	24.6	36.0				31.9	31.9
1939–1975	5.4	7.9				7.0	7.0
Universal winding							
1930–1975	4.1	4.1				8.4	N
Heavy weaving							
1930–1936	9.2	17.3	9.7	14.3	5.3	30.6	30.6
1937–1975	2.6	4.6	2.6	3.8	1.4	8.2	8.2
Draper weaving							
1930–1975	2.7	2.7				6.9	

N: No jobs within particular UJC.

TABLE 7. SUMMARY OF DOSE–RESPONSE RELATIONSHIPS FOR SELECTED CAUSES AMONG WHITE MALES ACHIEVING 15 OR MORE YEARS LATENCY

Cumulative dose (Fibre cm^{-3} days)	All causes			Diseases of the circulatory system (400–468)			Respiratory cancer lung cancer (162, 163)			Digestive system cancer (150–159)			Other nonmalignant respiratory diseases (510–527)		
	Obs.	Exp.	SMR	Obs.	Exp.	SMR	Obs.	Exp.	SMR	Obs.	Exp.	SMR	Obs.	Exp.	SMR
< 10 000	65	55.17	118*	21	24.37	86	8	3.59	223*	1	2.73	37	1	1.41	71
10 000– 40 000	57	32.83	174†	23	16.94	136*	7	1.96	357†	3	1.85	162	7	0.78	897†
40 000–100 000	32	13.63	235†	7	6.37	110	9	0.92	978†	3	0.79	380	7	0.38	1842†
100 000–200 000	6	3.42	175	1	1.30	77	2	0.13	1553*	0	0.16		2	0.08	2500*
Total	160	105.05	151†	52	48.98	106	26	6.51	399†	7	5.53	127	17	2.65	642†

*$p < 0.05$.
†$p < 0.01$.

40 000–100 000 fibre cm^{-3} days exposure group. Diseases of the circulatory system were statistically elevated only in the second dose category and demonstrated no consistent patterns of dose–response.

In contrast, strong dose–response trends were observed for both lung cancer and the disease group referred to as other nonmalignant respiratory diseases. For lung cancer, statistically excess mortality was observed in all exposure groups with an SMR for the low cumulative exposure category of 223 and 1553 for the highest exposure category. Although statistically significant, the SMR in the highest exposure category is based on only two deaths; thus, the SMR is unstable.

The SMR for other nonmalignant respiratory diseases was 71 in the lowest dose category; it rose to 2500 in the highest category. Statistically significant excesses were observed in all of the three highest dose groups. Again, the SMR in the highest group was based on only two deaths and stability of the SMR should be considered.

It is realized the SMRs for the four exposure groups may not be strictly compared with each other; however, it is useful to plot the dose–response data to observe patterns and trends. Such a plot is given in Fig. 2. The data points for the highest exposure category are not included since these were judged to be unstable.

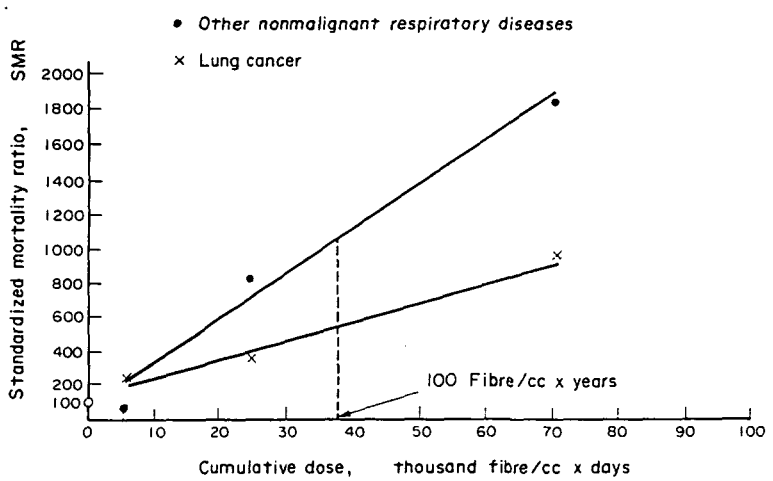

FIG. 2. Plot of lung cancer and other nonmalignant respiratory disease SMRs by cumulative dose, white males.

Although only based on three data points, Fig. 2 suggests a linear dose–response relationship for lung cancer with no threshold. The data for nonmalignant respiratory diseases are not as linear as lung cancer; however, the SMR rises much more steeply with increasing dose and may reasonably be described by a linear relationship.

DISCUSSION

Statistically excess mortality was observed for lung cancer and nonmalignant respiratory diseases among chrysotile asbestos textile workers. Furthermore, using cumulative dose as the exposure variable and the SMR as the measure of disease risk,

strong dose–response relationships were observed for both lung cancer and nonmalignant respiratory diseases. A linear relationship appears to adequately describe the form of the dose–response curve for both diseases. Lung cancer demonstrated a statistically significant excess in even the lowest cumulative exposure category of less than 10 000 fibre cm^{-3} days.

There are several factors which need to be considered in evaluating the occupational contribution to observed mortality patterns. The most important of these are the choice of standard population death rates to estimate expected deaths and cigarette smoking patterns among the cohort. Other potential confounders such as age, race, sex and calendar time period were dealt with in the study design.

The standard population death rates chosen for this study were those for white males for the entire U.S.A. Table 8 gives a comparison of lung cancer (ICDA 162, 163)

TABLE 8. COMPARISON OF LUNG CANCER MORTALITY RATES (ICDA 162, 163) BETWEEN COUNTY IN WHICH STUDY PLANT WAS LOCATED AND CONTIGUOUS COUNTIES, 1950–1969

	Age-adjusted deaths/100 000 White males
U.S.A.	37.98
State in which plant located	37.83
County in which plant located	66.5
Contiguous counties	
A	40.1
B	43.3
C	42.5
D	40.2
E	53.4
Counties one removed	
1	40.1
2	44.1
3	25.9
4	30.7
5	36.7
6	43.2
7	38.2

age-adjusted mortality rates for 1950–1969 for counties in the same area as the study plant with state and U.S. rates (MASON *et al.*, 1975). Lung cancer death rates for the state in which the plant was located were nearly equal to U.S.A. rates. On the other hand, rates for the county where the plant was located were 75% higher than U.S.A. rates for white males.

The choice of an appropriate comparison population for mortality analyses is difficult and arguments could be made for using rates for a set of counties contiguous to the county in which the plant was located. However, there are serious limitations to this approach which were considered in this study and resulted in rejecting the use of local county rates. First, the county in which the plant was located is the site of a large shipyard industry with peak employment of approx. 29 000 persons in 1943 (BLOT *et al.*, 1978). Employees for this industry were largely drawn from the local population.

Many of these workers are thought to have been exposed to asbestos during ship construction and repair. In an ecological study, BLOT *et al.* (1978) demonstrated an association between county lung cancer rates and shipyard employment. In a more refined case-control study, BLOT *et al.* (1979) demonstrated a summary odds ratio of 1.6 for shipyard employment and lung cancer after adjusting for smoking, other occupations, age, race and county of residence. These data suggest that lung cancer death rates in the area in which the plant was located are likely to be elevated by local shipyard employment.

A second factor to be considered in choosing local rates for comparison is the effect that the plant being studied might have had on local lung cancer death rates. Because of a lack of an employment record system prior to about 1930, it is difficult to estimate the exact number of persons ever employed at this plant; however, this is likely to exceed 10 000 prior to 1965. Thus number could have a significant impact on local lung cancer death rates, assuming an overall lung cancer SMR of 200 or more for these workers.

The effects of shipyard and asbestos plant employment make the use of local death rates inappropriate for this study. However, even if rates for contiguous counties had been used (Table 8) the expected lung cancer rates for white males would have been increased by only approx. 15%, not nearly sufficient to account for the observed excess lung cancer risk.

Cigarette smoking is a known risk factor for respiratory cancer and smoking and asbestos exposures have been shown to act in a synergistic manner to greatly increase the risk of lung cancer (HAMMOND *et al.*, 1978). Respiratory symptom questionnaires including questions on smoking history were administered by the U.S. Public Health Service to active workers in this plant in 1964 and again in 1971. In addition, smoking data available from plant medical records were also collected. While smoking histories are not available on all cohort members, these data are useful in estimating the prevalence of smoking in this plant for comparison with smoking patterns among U.S.A. males who were used as the standard population for estimation of expected lung cancer deaths.

The prevalence of cigarette smoking status among the asbestos study cohort is given in Table 9. These data largely represent the smoking prevalence found by the 1964 PHS survey, since cohort entry was limited to those achieving six months employment before 1965. The PHS 1971 data and company data were used only for those missed in 1964. Among white males, 52.4% were found to be current smokers, 25.3% non-smokers, and 22.3% past smokers.

Table 9 also compares smoking prevalence among the study cohort members with comparable data for U.S.A. adults (USPHS, 1979). These data show the prevalence of

TABLE 9. SUMMARY OF CIGARETTE SMOKING PATTERNS FOR WHITE MALE ASBESTOS TEXTILE WORKERS AND COMPARISON WITH DATA FOR U.S.A. WHITE MALES

	Current smoker (%)	Past smoker (%)	Non-smoker (%)
Asbestos workers ($N=292$)	52.4	22.3	25.3
U.S. white adult males (1965)	51.5	22.1	26.4

smoking among white males in the study cohort to be nearly identical to that of U.S.A. white males. The 22.3% prevalence of past smokers is also identical to U.S.A. figures. Available smoking data for this cohort suggest that the observed lung cancer and nonmalignant mortality excess among white males cannot be explained by cigarette smoking independent of asbestos exposure. This is supported by the dose–response data. While smoking cannot explain the observed lung cancer excess, an interactive effect with asbestos exposure is likely.

An important finding of this study is excess lung cancer and nonmalignant respiratory disease among workers exposed to chrysotile. There are few other published reports with which to compare the dose–response data obtained in this study. In fact, there are no other reports of dose–response using exposures expressed as fibres cm^{-3} by the phase contrast method; all other reports have used impinger (MPPCF) data (ENTERLINE and HENDERSON, 1973; MCDONALD *et al.*, 1980; ADVISORY COMMITTEE ON ASBESTOS, 1979). For comparison with other published data, approximate impinger exposure values, expressed as MPPCF yr, were calculated for data from the current study using the impinger–membrane filter conversions derived in this study. Estimated dose–response for lung cancer based on these estimates are given in Table 10, along with other published data.

The data in Table 10 show the SMR for lung cancer at a given cumulative dose for the present study to be much higher than other published values. However, there are differences in the designs of the three studies which may account for some of this apparent discrepancy. For example, the MCDONALD *et al.* (1980) study included persons exposed to extremely high airborne fibre levels; thus, competing risk may be a problem. The study by ENTERLINE and HENDERSON (1973) consisted of retirees 65 years or older. In the present study, only 6 of 26 lung cancer deaths were 65 or older. The ENTERLINE study may be a survivor population with less lung cancer risk for those surviving to age 65.

The current OSHA exposure standard of 2.0 fibres cm^{-3} is based on an allowable lifetime exposure of 100 fibres $^{-3}$ yr (i.e. 2.0 fibres cm^{-3} for 50 yr). Based on data from this study, elevated risks are predicted for lung cancer and for nonmalignant

TABLE 10. COMPARISON OF DOSE-RESPONSE RELATIONSHIPS FOR LUNG CANCER WITH OTHER PUBLISHED DATA

Present study		ENTERLINE and HENDERSON (1973)		MCDONALD *et al.* (1980)*	
Approximate MPPCF yr	SMR	MPPCF yr	SMR	MPPCF yr	SMR
<9.1	223				
9.1–36.5	357			30	104
36.5–91.3	978			100	114
		<125	168.2		
		125–249	224.5	300	142
		250–499	296.3	500	170
		500–749	500.0		
		>750	555.6		
				1200	268

*Based on cumulative exposures until age 45 yr. SMRs calculated from regression line provided by authors.

respiratory diseases at this exposure level. Of course, this is based on use of cumulative dose concept and ignoring any possible 'dose rate' effect as average exposures for most members of the cohort were considerably above 2.0 fibres cm^{-3}. Historic exposures at this plant have been considerably above 2.0 fibres cm^{-3}.

A noteworthy finding of this study is that only one of 191 deaths (0.5%) among white males was due to mesothelioma. It is possible that mesothelioma is underdiagnosed among this cohort and certain deaths mentioning 'cancer of the abdomen' are suspect. However, others have also found lower mortality due to mesothelioma among cohorts exposed only to chrysotile (MCDONALD *et al.*, 1971; NICHOLSON *et al.*, 1979; WEILL *et al.*, 1979). ROBINSON *et al.* (1979) observed 17 mesotheliomas among 1040 deaths in a plant using predominately chrysotile; however, some crocidolite and amosite were used in the plant.

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DISCUSSION

J. C. MCDONALD: You mention the close proximity of the naval yards of South Carolina. Could you say, of the 26 deaths of lung cancer on which this paper is based, what proportion of them has worked in the naval yards?

Dr DEMENT: We have information on only 10 of the 26 lung cancer cases and none of these was employed in the dockyards. However, if shipyard employment were to have a significant effect on observed mortality patterns, it should have a force of reversing the dose response patterns observed; e.g. those in the low cumulative dose category were short-term employees with greater possibility of having been exposed in the shipyards. Additionally, Dr A. McDonald observed (pp. 417–422) one mesothelioma in her group of South Carolina shipyard workers who were exposed to crocidolite. It would be rather surprising, if a high proportion of textile workers were employed in shipyards, to see only one mesothelioma in our textile worker cohort.

O. G. RAABE: I am uncomfortable with your use of the term 'dose' to describe exposure. For example, in your Fig. 2 should not the abscissa be more properly labelled 'cumulative exposure' instead of 'cumulative dose', since doses to the exposed individuals were not actually determined? The actual doses are related to the exposures in a complex way depending on conditions of deposition, particle aerodynamic-size and other unknown factors.

Dr DEMENT: Your point on dose is well taken. Unfortunately, this terminology has persisted in the epidemiological literature. In addition to exposure level and duration, dose for airborne dusts depends on patterns of pulmonary deposition and clearance. We have investigated airborne fibre characteristics in this plant using transmission electron microscopy and have estimated pulmonary deposition using the fibre deposition model published by Harris and Fraser. For these studies, airborne dust samples collected in 1964 by the membrane filter method were available. For the various plant textile operations, 10–27% of all airborne fibres were found to be longer than 5 μm in length. Using the deposition model, it was estimated that 13–15% of these airborne particles would be deposited in deep, non-ciliated portions of the lung and this is perhaps the true 'effective dose' portion of the exposure. Compared with other operations using chrysotile asbestos, such as the friction and cement product industries, textile operations were found to have a substantially higher fraction of long-thin fibres which Stanton and others have implicated as important for development of respiratory cancer.

L. SIMONATO: You explained in your paper the reasons for basing your expected death figures on national rather than county lung-cancer mortality rates. Did you, nevertheless, try to calculate SMRs on the basis of the county lung-cancer mortality rate?

Dr DEMENT: As Dr McDonald has pointed out, the county in which the plant is located is the site of a large naval shipyard with peak employment of approx. 29 000 persons in 1943. Two studies by our National

Cancer Institute have demonstrated a strong relationship between shipyard employment and lung cancer mortality in that county. The combined effects of the plant under study and this shipyard on local lung cancer rates make it highly undesirable to use rates from this one county in calculating expected deaths. Furthermore, as shown in Table 8 in our paper, neighbouring counties and the state as a whole have lung cancer death rates not significantly different from U.S. rates which were used to calculate expected deaths.

J. C. GILSON: Do you believe that relationships between the fibre counts and any other measures that were made in 1965 would still be appropriate for counts as made today? Although the membrane filter principle is still the same, I understand there have been considerable changes and improvements in the actual fibre counting.

Dr DEMENT: I think there have been more changes in fibre counting in the U.K. than in the U.S. The samples in 1964 were collected by the Public Health Service by the method they then recommended; the same methods are still used at the present time in the U.S.

H. WEILL: Although your results depend critically on conversion factors between particle counts (in mppcf) and fibre counts (in f/ml), I will leave comment on this to our dust physicist colleagues. However, since you showed us that impressive picture of a carding machine taken in 1938 and you have estimated that the operators in that area were then exposed to five or six fibres/ml, I would suggest that a careful re-assessment of the past exposure estimates in this cohort should be made. Secondly, I am quite surprised that your asbestos mortality risk exceeds the lung-cancer mortality risk and has a steep dose–response slope. While I am prepared to accept that this might be the case if asbestos *morbidity* was assessed by radiographic or lung-function measurements, the demonstrated *death* rates for asbestos would, in my view, be very unexpected at the estimated levels of exposure in your population.

Dr DEMENT: Mortality is obviously not the best way to study non-malignant diseases such as asbestosis. If one looks closely at the distribution of deaths from non-malignant respiratory diseases in our study, a deficit of deaths is noted except for rubrics 510–527; the deficit for pneumonia was significant. It is probably legitimate to look at all non-malignant respiratory diseases as a group, since it is likely that, once an asbestos worker is diagnosed as suffering from asbestosis, his pneumonia death is likely to be coded as asbestosis for the underlying cause. Studies of chest films and lung function are more appropriate for study of asbestosis. A chest film reading trial for this cohort is now being considered. However, the steeper slope for pneumoconiosis vs lung-cancer mortality is not surprising and has been found by others including MCDONALD *et al.*, in their studies of Quebec chrysotile miners and millers and ROBINSON *et al.*, who studied factory workers exposed to predominantly chrysotile.

Your other point concerned the low levels of exposure in carding. With the help of the company involved, we have made a careful assessment of exposures in this plant, including documentation of process and control system changes between 1930 and 1975. In assessing exposure levels one must look at the whole picture. In carding, controls were in place at the time of the 1938 U.S. Public Health Service study and these same carding machines and controls remained in place until 1975, the end of our study. Over this time period, hundreds of samples were collected in carding and these data are reflected in the exposure estimates. Additionally, during the 1938 U.S. Public Health Service study, efforts were made to simulate exposures before controls were in place by shutting off the ventilation systems. Measurements made without ventilation were two and three times higher than those with controls and, in fact, closely simulated insurance company exposure data collected in this plant before controls were in effect. These data are remarkably consistent and supportive of our exposure estimates. Our exposure estimates are also in line with data published by Lynch and Ayer in 1966 where fibre exposure levels in nine textile milling operations covering a large cross-section of this industry were investigated. Exposure levels in those plants with poorest controls closely approximate levels estimated for the plant under study prior to full application of control measures in about 1940.

F. D. K. LIDDELL: Table 10 makes an attempt to put the current findings in context with previous exposure/response relationships for lung cancer. In the studies by MCDONALD *et al.*, of Canadian chrysotile miners (*Br. J. ind. Med.* 1980, **37**, 11–24) the asbestos dust exposure was accumulated up to age 45 yr. The deaths were those which occurred after age 45 and before the end of 1975, and person-years were included only after age 45 following the principles discussed by LIDDELL *et al.* (*Jl R. statist. Soc.* Series A 1977, **140**, 469–491). Did the present authors use the same principle, i.e., classify men by the exposure accumulated in the first 15 yr since initial employment, and then count person-years, and deaths, from that point in time for each individual?

Comment is also needed on the high lung-cancer SMRs for the lowest exposure groups in the studies of asbestos factory workers. Enterline and colleagues (ENTERLINE, P. E., DECOUFLE, P. and HENDERSON, V. An epidemiological study of respiratory cancer among retired asbestos workers to establish standards for occupational exposure. Presented at the Annual Meeting of the American Academy of Occupational Medicine, Pittsburgh, Pennsylvania, 9 February 1972) quoted a 'completely parallel study of 324 male retirees who worked as production or maintenance employees in the manufacture of a variety of building materials and were exposed to some dust, none of which contained asbestos or any substance suspected as being carcinogenic'; here there were nine lung-cancer deaths, with SMR = 169.8. It seems most realistic to take as base either the SMR for the group with the least severe exposure or the almost identical SMR for the unexposed men; for those exposed to at least 500 (mmpcf × years) the SMR (= 519) was 3.1 times that for those exposed to less than 125 (mmpcf × years). The similarity to the corresponding figure from Quebec is surprising when it is borne in mind that some of Enterline's subjects had been exposed to amphibole and that the epidemiological methods were rather different. In the current study, it seems most unlikely that lung cancer mortality among men exposed to less than 9.1 (mmpcf × years) could truly have been well over double the 'normal'. Nevertheless, for those in the two most severe exposure groups combined, i.e. 36.5–182.6 (mmpcf × years), the SMR, on the basis presented, was 100 (9 + 2)/(0.92 + 0.04) = 1146, or 5.1 times that for those exposed to less than 9.1 (mmpcf × years). This gradient is steeper, by at least an order of magnitude, than in other chrysotile studies, where a factor of 5 could be associated only with enormously heavier exposures.

Dr DEMENT: The dose–response analyses were done using methods employed by LUNDIN *et al.* (1971) and further described by BRESLOW (1976) as referenced in the report. Cumulative fibre exposure strata were created without any prior knowledge of the mortality outcome. During the course of the follow-up period of 1940–1975, a worker was moved from one stratum to another as his cumulative exposure increased; thus, a worker contributed person-years and expected deaths in several exposure strata while contributing observed death to only the highest stratum achieved. Exposures were accumulated during the first 15 yr since initial employment; however, person-years and deaths were only counted from 15 yr onward. This was done to insure a minimum latency period of 15 yr for lung cancer.

Comment is made on the high lung-cancer SMR for the lowest exposure group and it is suggested that this may be an anomaly of the study design. We do not believe this to be the case. The data presented at this conference concerned workers employed more than 5 months in textile operations. We are continuing to follow up a cohort of approximately 500 textile workers at this plant employed 1–6 months. Follow-up is nearly complete for this group and five lung cancers have been observed vs four expected, resulting in a lung-cancer SMR of 125. These data follow the dose–response patterns presented in Table 7 and Fig. 2 of our paper and provide information on a sizeable cohort having lower lifetime cumulative exposures. The low lung-cancer SMR in this group suggests the control population is appropriate.

S. RICHARDS (written question): (1) Much of the data in the paper is based on impinger samples. Are the expressed dust levels personal ones or do they relate to areas? (2) Page 881 states 'In fact, there are no other reports of dose–response using exposures expressed as fibres cm^{-3} by the phase contrast method; all other reports have used impinger (MPPCF) data (ENTERLINE and HENDERSON, 1973; MCDONALD *et al.*, 1980; ADVISORY COMMITTEE ON ASBESTOS, 1979)'. The latter report surely uses impinger data but expresses its conclusions as fibres cm^{-3} by the phase contrast method. Indeed, my understanding is that membrane filter counting was available from about the same time as in the Dement study.

Dr DEMENT: As in most studies of this type, the available industrial hygiene sampling data were comprised of both area and personal breathing zone samples. Fortunately, much of the early impinger data collected by the company insurance carrier, the U.S. Public Health Service and the company industrial hygienist were breathing zone samples. The exposure models which were developed took into account the difference between general area samples and breathing zone samples in estimating exposures. For instance, the exposure estimates for machine operators were taken as the average of all samples within a given area plus an 'increment' in exposure attributable to a specific job. This 'increment' was estimated using breathing zone and personal samples. The data given in Table 6 demonstrate these estimates. In the fibre preparation/waste recovery operation for the period 1930–1944, the overall average area exposure was estimated to be 26.2 fibres cm^{-3}. However, average exposure for operators, clean-up personnel and persons handling raw fibre ranged from 35 to 78 fibres cm^{-3} or 1.3–3.0 times the area average. These data are consistent with other data concerning the ratio of personal to static samples in asbestos processing operations.

The statement concerning the lack of other reports of dose–response using exposures expressed as fibres cm^{-3} was meant to be other published articles dealing with lung cancer. The 1979 report by Her

Majesty's Stationery Office made estimates using various impinger/membrane conversions but relied on published dose–response data expressed as mppcf × years. A preliminary report of lung-cancer dose–response using fibre estimates was presented by McDONALD *et al.* at the Lyon conference of the 'Biological Effects of Mineral Fibres' sponsored by the IARC. It is interesting to note that an average conversion factor of 3.14 was estimated by McDONALD *et al.* for the impinger/membrane filter conversion.

A. L. RICKARDS (written comment): The authors of this paper should be complimented for undertaking a difficult project and presenting an excellent paper. However, the paper raises several questions which, it should be emphasized, are not unique to the particular presentation.

First, it is relevant to question whether the relationship between modern membrane filter and modern impinger counts can be applied to historical impinger data, recognizing that modern dusts are *believed* to contain a lower proportion of coarse particulates, arising from improved processing at the mines. In this context the limitations of the optical system and the counting cell used in conjunction with the impinger, and the consequent insensitivity to fine particulates, must be recognized. The photographs illustrating early operations in the plant strongly suggest that the dust levels have been underestimated. Such a tendency could occur if the ratio of fine to coarse particulates had altered over the years.

The second topic which should be given consideration is that of personal exposure compared with static monitoring. It is well known that many jobs within the textile industry demand close contact with both machine and product and consequently careful consideration should be given to job practices when allocating exposure values derived from static monitoring. It is also known that different 'qualities' of product can influence dust exposure. The background or static sample result might crudely represent a mean exposure value within a work area. However, if the range of exposures is large, which is likely in a 1950s' textile plant, then it is surely necessary to acquire a working knowledge of the exposures in the upper half of the range. A background sample of 10f ml^{-1} could readily represent a range of exposure from 2 to 40f ml^{-1} and possibly higher, depending upon job practices. Fibre counting errors should also be considered, especially if the samples were too dense for ideal counting. Static sampling data, especially those derived from grab samples, are unlikely to provide estimates of these upper exposures directly, especially if the results are averaged, and therefore a full understanding of job practices would be of great value. For instance, the jobs at carding would include the relatively dust-free function of attending the front of the machine, perhaps represented by the static sample. Other operations would include loading the hopper at the rear of the machine, off-loading the bobbins of sliver and at intervals lying upon the floor to remove accumulated fibre from the area underneath the machine, in addition to running maintenance. There are cleaning down operations and breakdown situations to consider. All of these operations would be adding significantly to the actual dust exposure compared with that recorded by a background sampler located at some position distant from the job operation.

A third and important aspect is that early monitoring systems were not designed to measure exposure for epidemiological purposes. They are intended to monitor the effectiveness of engineering control measures and probably served this purpose well.

Dr DEMENT: The relationship between membrane filter and impinger counts is critical for the dose–response relationships derived in our study. The question being raised is whether or not the conversion derived for more recent samples applies to past impinger counts made in the 1930s and 1940s.

First, two independent sources of data were available for estimating the conversions: 120 paired impinger-membrane filter samples collected in 1965 and 986 concurrent samples by these two methods in plant operations collected during 1968–1971. Admittedly, these two sources are not separated far temporally, but similar conversions were obtained from the two data sets. Variations in conversion factors with time were investigated in the linear models used to study the 1968–1971 sample data and no significant trends were observed.

Mr Rickards suggests that changes have taken place in the nature of asbestos fibres received in textile mills and this may affect impinger/membrane filter conversion factors. The most important change has been the degree of fibre opening done at the mine site vs the textile mill. In this plant, crude unopened fibre was processed using pan crushers until approx. 1965. A major function of the preparation operation is to remove non-fibrous particulates and short fibres. Changes in the nature of asbestos fibres received at the textile plant would likely affect only the conversion in preparation and not subsequent textile operations. This finding is supported by both data sets used for conversion estimates, where only preparation was found to have a significantly different conversion factor. Fot the current study a conversion of 8 was used for preparation vs 3 for other operations. This is probably a high estimate for preparation even for samples in the 1930s and 1940s.

Mr Rickards also questioned the use of static samples for estimating personal exposures and the usefulness of early monitoring data for epidemiological purposes. As discussed in our response to Dr Richards' questions, an account was made for differences between static and personal sampling in our

exposure estimates. This plant is unique in having available a considerable quantity of early breathing zone exposure data collected in a systematic manner. These sources included early insurance company data, U.S. Public Health Service data collected during 1930–1940 and the company sampling programme which began in 1956. The company sampling programme was unique in that a sampling network was established which consisted of sampling stations adjacent to machine operators in an attempt to approximate breathing zone exposures. These stations were assigned an identification number and breathing level samples collected on a routine basis at these sites from 1956 to 1971. Additional breathing zone samples were collected for mobile personnel. The systematic manner in which these data were collected over a long period of time, in addition to excellent coverage of all plant operations, makes these data most useful for epidemiological purposes. It should also be pointed out that data generated to monitor the effectiveness of engineering controls probably overestimate exposures, since samples are generally collected where known or suspect problems exist. (See also discussion of paper by NEWHOUSE *et al.*, pp. 899–909.