Development of a Fiber Size-Specific Job-Exposure Matrix for Airborne Asbestos Fibers

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Title:

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ABSTRACT

Objectives: To develop a method for estimating fiber size-specific exposures to airborne asbestos dust for use in epidemiologic investigations of exposure-response relations.

Methods: Archived membrane filter samples collected at a Charleston, SC asbestos textile plant during 1964-1968 were analyzed by transmission electron microscopy (TEM) to determine the bivariate diameter/length distribution of airborne fibers by plant operation. The protocol used for these analyses was based on the direct transfer method published by the International Standards Organization (ISO), modified to enhance fiber size determinations, especially for long fibers. Procedures to adjust standard PCM fiber concentration measures using the TEM data in a job-exposure matrix (JEM) were developed in order to estimate fiber size-specific exposures.

Results: A total of 84 airborne dust samples were used to measure diameter and length for over 18,000 fibers or fiber bundles. Consistent with prior studies, a small proportion of airborne fibers were longer than >5 μm in length, but the proportion varied considerably by plant operation (range 6.9% to 20.8%). The bivariate diameter/length distribution of airborne fibers was expressed as the proportion of fibers in 20 size-specific cells and this distribution demonstrated a relatively high degree of variability by plant operation. PCM adjustment factors also varied substantially across plant operations.

Conclusions: These data provide new information concerning the airborne fiber characteristics for a previously-studied textile facility. The TEM data demonstrate that the vast majority of airborne fibers inhaled by the workers were shorter than 5 μm in length, and thus not included in the PCM-based fiber counts. The TEM data were used to develop a new fiber size-specific JEM for use in an updated cohort mortality study to investigate the role of fiber dimension in the development of asbestos-related lung diseases.

BACKGROUND

While a causal association between exposure to asbestos and the risk of lung cancer, mesothelioma, and non-malignant pulmonary diseases in humans has been well established, the relative contribution of airborne fibers of different dimensions is not well defined. Asbestos fiber inhalation, implantation, and injection studies in experimental animals have generally shown long-thin fibers to be more biologically active in the production of lung cancers and mesotheliomas [1-3]. Additionally, some data suggests that the risk for lung cancer, mesothelioma, and asbestosis may vary by both fiber type and fiber dimensions [4].

Epidemiological studies have not directly addressed fiber size-specific risks due to limited data that characterizes the joint diameter and length distributions of asbestos aerosols. Exposure concentrations determined by phase contrast microscopy (PCM) and integrated over a working lifetime are strong predictors of asbestosis and cancer risks within a given industry; however, differences in risks between industry sectors (e.g. chrysotile mining versus textiles) have not been reconciled by the PCM method. The PCM method measures only a limited portion of the aerosol (i.e. fibers > 5 μm in length) and has a limit of resolution of approximately 0.25 μm, which means that many airborne asbestos fibers will not be counted, even though many of those with diameters

<0.25 µm are longer than 5 µm (length of fibers counted by PCM). Limitations of the PCM method suggest that a more predictive exposure-response relationship might be observed in epidemiologic studies using a fiber size-specific exposure metric based on transmission electron microscopy (TEM), which can measure the entire asbestos aerosol.

TEM analyses of airborne chrysotile fibers in different industries have shown reasonably large differences in fiber length and diameter distributions [5]. Airborne chrysotile fibers in mining and milling demonstrate a significantly greater percentage of fibers (95-98%) less than five micrometers in length compared to data from textile facilities using chrysotile[5 6 7]. TEM data also show considerable variation in fiber size distributions among different operations within the same industry [5 7 8]. Data for asbestos textile plants using chrysotile have shown initial operations such as fiber preparation and carding to produce airborne fibers with a greater proportion of the fibers > 0.25 µm in diameter and > 5 µm length compared to subsequent operations such as spinning, twisting, and weaving [5]. This is expected as fiber preparation and carding remove much of the debris and shorter fibers and subsequent operations impart energy to open fiber bundles. Consistent with variability in fiber size by textile operation, our prior analyses have suggested differences in lung cancer risks by textile department after controlling for cumulative exposures by PCM.[9]

The current research aims to expand upon our prior studies by using TEM data to develop a fiber size-specific job-exposure matrix (JEM) for use in epidemiologic studies of Charleston, South Carolina, USA asbestos of textile workers [9 10]. Samples for these TEM studies were obtained from an archive of membrane filter samples collected in these plants by the U.S. Public Health Service (USPHS).

REVIEW OF ALTERNATIVE EXPOSURE METRICS

The impinger method for measurement of airborne dusts, including asbestos, was developed by the USPHS in the 1920's and measured all particles less than 10 µm in diameter (i.e. those considered respirable) by low power, optical microscopy and expressed dust concentrations as millions of particles per cubic foot of air (mppcf) [11]. In the 1960's the impinger began to be replaced by the membrane filter sampling method with counts of fibers longer than 5 µm being done by phase contrast optical microscopy (PCM) and with fiber concentrations being reported as fibers longer than 5 um per cubic centimeter of air (fibers/cc) [12-15]. The PCM method is considered a better predictor of disease risks compared to concentrations of all airborne particles by the impinger method [15] and serves as the basis for current risk assessments for occupational asbestos exposures, as well as for sampling for compliance with U.S. occupational and environment regulations.

Animal data strongly suggest that longer-thinner asbestos fibers may be more biologically active and that risks may vary by disease endpoint [16-19]. Lippmann [19] reviewed published data and concluded that asbestosis is most closely related to the surface area of retained fibers that are between > 0.15 and < 2.0 µm in diameter, that mesothelioma is most closely associated with numbers of fibers longer than approximately 5 µm and thinner than approximately 0.1 µm, and that lung cancer is most closely associated with fibers longer than approximately 10 µm and thicker than approximately 0.15 µm. Berman et al. [18] and Berman and Crump [20] reanalyzed data from inhalation studies in AF/HAN rats and concluded that structures most predictive of lung tumor risk appeared to be long (>5 µm) thin (<0.3 µm) fibers and bundles, with a possible contribution by very long (>40 µm) and

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very thick (>5 μm) complex clusters and matrices. However, their statistical model assigned weights to some fiber size categories (i.e. >5 µm in diameter) that would have a very low probability of deposition in rat lungs [21-22].

Quinn et al. [23] suggested alternative fiber exposure metrics based on fiber size and composition for man-made vitreous fibers. These indices were collectively called the 'Hypothetically Active Fiber (HAF) Indices'. These authors calculated various HAF indices based on biologically important fiber sizes suggested by Stanton, Pott, and Lippmann [16 17 19] as well as their own and compared these to PCM fiber measures. No consistent relationship among these measures was observed and the index of fibers hypothesized to be relevant for a study of lung cancer risk was not found to equate to the standard fiber PCM concentration measures. Quinn at al. developed and applied a method to adjust standard fiber concentration measures to the biologically relevant HAF concentrations using proportions from bivariate diameter/length fiber size distributions [23 24].

METHODS

TEM Size-specific JEM Conceptual Model

Dement et al. [8 25 26] developed a JEM for a Charleston, South Carolina asbestos textile plant based on fiber concentrations determined by PCM. Airborne dust samples (n=5952) covering the period 1930-1975, were used to fit parameters of statistical models to predict mean PCM concentrations by department, job, and calendar time period. For purposes of model development, the plant was divided into 10 exposure zones that corresponded closely to textile departments (e.g. fiber preparation, carding, spinning, twisting, weaving, finishing, etc.) based on the similarity of processes and characteristics of exposures. Within each exposure zone, jobs were further divided into four or more uniform job categories (UJC) in order to capture differences in PCM concentrations by job tasks within zones. Changes in concentrations by calendar time were accounted for in the models by inclusion of covariates for changes in processes or engineering controls based on plant records. The resulting JEM demonstrated substantial differences in airborne fiber concentrations by exposure zone, job, and calendar time period and has been used extensively in prior risk assessments in this plant [8 9 10]. An example of the JEM for mean PCM concentrations and confidence intervals by job category and time period for zone 1 (Fiber Preparation) is shown in Table 1 [26].

TABLE 1
PCM EXPOSURES FOR ZONE 1 (FIBER PREPARATION)

Uniform Job Category	Mean PCM Fiber Concentration (Fibers > 5 µm/cc) and 95% CI		
	1930-1944	1945-1964	1965-1975
A: General Area Personnel	26.2 (12.1-40.2)	8.1 (6.0-10.1)	5.8 (4.4-7.2)
B: Machine Operators Fly machine operator	78.0 (38.1-117.8)	23.9 (17.7-30.2)	17.2 (13.1-21.3)
Crusher operator	78.0 (38.1-117.8)	23.9 (17.7-30.2)	17.2 (13.1-21.3)
Waste machine operator	45.9 (21.0-70.8)	14.1 (9.5-18.7)	10.1 (4.4-19.6)
C: Cleanup Personnel	54.4 (10.7-98.1)	16.7 (5.4-28.0)	12.0 (4.4-19.6)
D: Raw fiber handling	35.0 (17.0-53.0)	10.8 (7.3-14.2)	7.3 (5.7-9.0)

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The airborne fiber size-specific JEM developed for the current project was based on the prior JEM published by Dement et al. [8][26] for the Charleston plant and incorporated the same exposure zones and UJCs. Our fiber size-specific JEM is based on the 'adjustment factor' method proposed by Quinn et al. [23], which 'adjusts' standard fiber concentration measures determined by PCM to the biologically relevant size-specific fiber concentrations using proportions from bivariate fiber size distributions. Within a given plant exposure zone, TEM airborne fiber diameter/length distributions for UJCs within the zone were similar; therefore, TEM samples within a given exposure zone were combined to arrive at an overall estimate of the zone-specific bivariate diameter/length distribution [8][9][26]. The decision to combine samples within zones was also based on the limited number of archived samples by job within zones and available resources for TEM analyses.

Based on the adjustment factor method for PCM concentrations developed by Quinn et al.[23], PCM adjustment factors by fiber diameter and length category can be expressed as follows for a given plant exposure zone:

$$\text{PCM Factor}_{ijz} = [(F_{ijz})/(FPCM_i)]$$

Where:

PCM Factor_{ijz} = PCM to TEM conversion factor for exposure zone 'i', fiber diameter category 'j', and length category 'z'. This factor, when multiplied by the estimated mean PCM concentration for a given zone, job, and time period from Dement et al. [26], results in a fiber size-specific exposure estimate.

$FPCM_i$ = Proportion of all airborne fibers measured by TEM which are actually counted by PCM (>0.25 µm in diameter and >5.0 µm in length) for exposure zone 'i'.

F_{ijz} = Proportion of all TEM fibers in exposure zone 'i', which fall into fiber diameter category 'j', and length category 'z'.

The proportion of all airborne fibers of a specific size determined by TEM (F_{ijz}) was estimated from the final TEM bivariate diameter/length matrix for each exposure zone. The model parameter $FPCM_i$ was calculated from the diameter/length matrix using estimates of the proportion of all airborne fibers measured by TEM that are actually counted by PCM (>0.25 µm in diameter and >5.0 µm in length). In order to derive a summary exposure metric such as the one proposed by Stanton [17] (i.e. fibers < 0.25 µm in diameter and >8.0 µm in length) for a given exposure zone 'i', the PCM factors for the desired TEM size categories are multiplied by the estimated PCM concentrations from Dement et al. [8][26] and summed. Similar procedures can be used to derive exposures metrics based on multiple combinations of TEM fiber length and diameter, the size-specific JEM thus allows considerable flexibility in defining fibers size categories of interest.

Membrane Filter Samples

In order to develop the fiber size-specific JEM, TEM data were used to define the bivariate diameter/length distribution of fibers using archived air samples. Historical membrane filter dust samples collected by the USPHS during industrial hygiene studies of the Charleston plant were used.

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A total of 203 archived samples were located for the present study. These archived samples were collected over the time period 1964 -1968; therefore, an inherent assumption in development of the JEM is that airborne fiber size characteristics have remained substantially the same over a study period covering the late 1930's through the end of asbestos textile production in approximately 1977. This assumption is reasonable since production methods and equipment remained essentially unchanged over this time frame and engineering controls for asbestos dust were first installed in the 1930's [8][26]. Additionally, the major chrysotile asbestos fiber source (Canada) remained unchanged during this period. In contrast, the airborne fiber concentrations were shown to vary by calendar time, and workers' PCM-based exposure estimates were based on several thousand industrial hygiene samples collected from 1930's to 1975.[26]

All archived membrane filter samples were matched to their original field data sheets in order to assign samples to the same exposure zones and uniform job categories developed by Dement et al. [8][26]. Based on available resources and available archived samples, a stratified random sample of 86 membrane filters was selected with sampling strata defined by the ten exposure zones. When only a few archived samples were available for a specific exposure zone, all usable samples for that zone were used for TEM analysis.

TEM Methods

Published TEM analysis and structure counting protocols were reviewed in order to select the protocol most suitable for the current study [27-30]. Criteria established for evaluation and selection of methods were as follows:

1. Preservation of Airborne Size Characteristics: The method must preserve the characteristics of the asbestos fiber aerosol present in the facility sampled and deposited on the membrane filter. Direct transfer preparation methods better preserve the original airborne fiber characteristics [27].

2. Enumeration of Fibers and Structures by Morphology: The method should allow airborne fibers to be characterized as to individual fibers, fiber bundles, and more complex entities such as matrices and clusters.

3. Prior Use in Risk Assessments: Use of the TEM method for human or animal study risk assessments was considered desirable but not a required criterion.

Published TEM methods differ in the procedures incorporated for sample preparation and the manner in which asbestos structures are counted. The ISO direct transfer method represents progressive improvements in the earlier TEM methods for enumerating asbestos structures and their morphology. Moreover, this method has been used in fiber size-specific risk assessments of animal bioassay data [18]. The ISO method thus represented the best choice for the current investigations based on the criteria outlined above.

Our analyses used the ISO allowed minimum aspect ratio of 3:1 to define fibers and structures for consistency with PCM methods. Several modifications and enhancements to the ISO method were made for this study [31]. These changes were needed to accommodate use of historical samples, with

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relatively high dust loadings, and to enhance estimation of the bivariate diameter/length distribution of the airborne aerosol, especially for longer fibers (which represent a relatively small proportion of the fiber size distribution). These modifications and enhancements were as follows:

1. In order to accommodate sizing of the large number of fibers needed for this study, diameter and length were recorded into discrete categories (rather than exact measurements of each fiber dimension) to increase the efficiency and reduce the cost of analyses. Fiber length was recorded into categories with widths increments of 0.5 μm for the count of all structures (20,000X magnification) and in 1 μm increments for the > 5 μm and > 15 μm structure counts (10,000X magnification). Fiber diameter was recorded in size categories with increments of 0.25 μm for all sample strata. These categories were later collapsed into larger categories for the JEM.

2. The ISO stopping rule for dispersed matrices and dispersed clusters was not used and all visible fibers and fiber bundles within these structures were enumerated and sized. This enhancement allowed us to better define the true diameter/length distribution.

3. For each sample, three separate analyses were performed, based on fiber length, in order to increase the count of the less-prevalent longer fibers and therefore achieve greater statistical precision of the bivariate size distributions. These analyses consisted of counting all structures, structures > 5 µm and structures > 15 µm. The stopping rules (i.e. *minimum* number of *primary* structures to be sized and recorded) were:
    a. all structures: 50
    b. structures longer than 5 µm: 80
    c. structures longer than 15 µm: 50

A primary structure is a fiber or connected group of fibers (with or without other particles) that is a separate entity in the TEM image [27]. In developing this JEM, the individual fiber or fiber bundle data were used, whether these were present as components of complex primary structures or as individual primary structures [18]. For each counting stratum, the number of grid openings used to obtain the desired structure count was recorded. The TEM data for each sample were recorded in Microsoft Excel worksheets based on the ISO method [27] but designed for this study and imported into SAS Version 8.2 [32] for statistical analyses.

TEM Data Reduction and Analyses

TEM samples within a given exposure zone were combined to arrive at an overall estimate of the zone-specific bivariate diameter/length distribution. Samples within each zone were combined based on pooling the fibers counted within TEM counting strata (all structures, structures > 5 µm, and structures > 15 µm). TEM fibers with a minimum aspect ratio of 3 to 1 were reduced to a matrix containing 20 categories based on diameter and length, including fiber diameters of <0.25, 0.25-1, 1-3, and >3 µm and fiber lengths of <1.5, 1.5-3, 3-5, 5-15, 15-40, and >40 µm. The smallest diameter category measured by TEM varied slightly due to small fluctuations in TEM calibration, with a nominal value of 0.25 µm. These size categories were selected *a priori* based on consideration of both biological and measurement/analysis factors, including critical sizes for PCM (0.25 µm width, 5 µm length), fiber deposition in human lungs (~3 µm width) [33 34], lung clearance

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(~15 µm) [35], previous risk analysis (40 µm) [18], and additional cut-points to divide the width and length distributions into reasonably populated cells, given the distribution known to be skewed toward shorter fibers based on previous studies (<1 µm width; <1.5 and 3 µm lengths). However, data analyses methods developed for this study allow researchers to specify different choices for diameter and length depending on the research question.

Within each TEM counting stratum (all structures, structures > 5 µm, and structures > 15 µm), the fiber counts were combined and the proportional distribution by diameter/length category calculated directly as a simple proportion. The bivariate diameter/length proportion was calculated as the sum of the cell counts divided by the total number of fibers counted within the TEM counting stratum. The all structure stratum thus provides an estimate of the overall bivariate diameter/length distribution whereas proportions calculated from the >5 µm, and >15 µm strata can be viewed as conditional or truncated distributions, conditioned on first meeting the minimum fiber length to be counted. Overall bivariate diameter/length cell proportions were calculated using the expression below. These calculations were used for all fiber diameters within a given strata based on products of conditional probabilities derived from the pooled data for each exposure zone:

For fibers less than or equal to 5 µm in length :

Cell Proportion = Cell proportion calculated using the pooled all structures TEM counting stratum.

For fibers > 5 µm in length and up to 15 µm in length:

Cell Proportion = (Proportion > 5 µm in length calculated from the pooled all structures TEM counting stratum) * (Cell proportion > 5µm but <15 µm in length calculated from the pooled > 5 µm TEM counting stratum).

For fibers > 15 µm in length:

Cell Proportion = (Proportion > 5 µm in length calculated from the pooled all structures TEM counting stratum) * (Proportion > 15 µm in length calculated from the pooled > 5 µm TEM counting stratum)*(Cell proportion calculated from the pooled > 15 µm TEM counting stratum).

This method efficiently used each successive TEM counting stratum to better estimate the bivariate proportion of longer fibers without restrictive distributional assumptions. Bootstrapping was used to estimate statistical variability for the proportion of airborne fibers in each diameter/length category and the PCM adjustment factor ($F_i/FPCM_i$) for each cell. For each pooled stratum (all structures, structures > 5 µm, and structures > 15 µm), we randomly selected structures from each TEM counting stratum, with replacement, with the stratum sampling frequency being equal to the pooled structure count for the exposure zone. This re-sampling procedure was replicated 500 times for each zone. For each replicate, an estimate of the proportion of all TEM structures countable by PCM (>0.25 µm diameter and > 5 µm in length), the mean proportion of fibers in each diameter/length category of the matrix, and the size-specific PCM adjustment factor ($F_{ijz}/FPCM_i$) were calculated. Using the data from each of the 500 replications, the mean proportion of fibers and the PCM adjustment factor ($F_{ijz}/FPCM_i$) were calculated for each diameter/length category of the matrix as well as lower 5% and upper 95% confidence intervals using the bootstrap percentile method [36]. An exposure metric based on approximations of fiber surface areas was developed in a like manner. For this metric, we assumed that fibers and fiber bundles could be considered right cylinders and

calculated the surface area (μm^2) for each structure counted. For each of the 500 replications described above, we calculated the mean surface area for each diameter/length category and a PCM to surface area adjustment factor. The distribution of the parameter estimates from the 500 replications was used to estimate the standard deviations of the surface area factor by diameter/length category and to construct lower 5% and upper 95% confidence intervals. The PCM surface area adjustment factor represents a multiplier to be used with PCM concentrations to express concentrations in terms of surface area (μm^2/cc). This should be viewed as a relative rather than absolute surface area measure, useful for internal comparisons within this cohort, due to the simplifying assumption that fibers were right cylinders.

Analyses presented in this report are based on fibers and fiber bundles identified as individual structures or as components of larger structures. Precise measurement of chrysotile fiber diameter is challenging, especially for fibers bundles with varying diameter along their length and for fibers identified as components of more complex matrices. However, our quality control analyses demonstrated good reproducibility with regard to assignment of these structures into the diameter and length categories used for this study.

RESULTS

Two of the 86 samples were determined not to be unusable due to extremely low fiber densities, resulting in very few structures being counted and sized based on stopping rules for the TEM method, so TEM data were obtained from 84 filters. The distribution of samples included in the study by exposure zones and associated plant departments is shown in Table 2. The number of samples available for TEM analyses ranged from 3 to 11 by exposure zone. A total of 18,824 fibers or fiber bundles were enumerated and included in the analyses.

TABLE 2

SAMPLES ANALYZED BY TEM BY ZONE AND DEPARTMENT

Exposure Zone	Plant Department Associated with Exposure Zone	Number of TEM Samples
1	Preparation	6
2	Carding	11
3	Ring Spinning	11
4	Mule Spinning	11
5	Foster Winding	5
6	Twisting	6
7	Universal Winding	9
8	Heavy Weaving	11
9	Light Weaving	11
10	Finishing Operations	3

Considerable differences in the fiber length and diameter distributions were observed by exposure zone (Figures 1 and 2). The proportion of fibers longer then 5 μm ranged from 6.9% (95% CI=3.9-9.8) in zone 10 (Finishing) to 20.8% (95% CI=18.7-22.8) in zone 7 (Universal Winding). The proportion of fibers <0.25 μm in diameter but with lengths >5 μm, and not generally detectable by PCM, was found to range from 4.5% (95% CI=6.7-12.8) in zone 10 (Finishing) to 11.4% (95% CI=10.1-12.5) in zone 4 (Mule Spinning). In most plant exposure zones, only a small proportion of airborne fibers were longer than 15 µm, with a range of 1.7% (95% CI=0.8-2.7) in Finishing operations to 6.2% (95% CI=5.3-7.2) in Universal Winding.

The overall bivariate fiber diameter/length distribution for the Charleston plant is given in Table 3. This table provides the proportion of all airborne fibers within each cell of the diameter/length matrix, the PCM adjustment factor ($F_{ijz}/FPCM_i$), and statistical confidence intervals for these parameters. These same estimates were generated for each exposure zone (not shown).

TABLE 3
BIVARIATE FIBER SIZE DATA AND PCM ADJUSTMENT FACTORS
OVERALL PLANT SUMMARY

Fiber Diameter µm	Fiber Length µm	Fibers Sized	Proportion of All Fibers by TEM	Lower 5% of Cell Proportion	Upper 95% of Cell Proportion	PCM Adjustment Factor	Lower 5% of PCM Adjustment Factor	Upper 95% of PCM Adjustment Factor
<0.25	<1.5	5061	0.486	0.479	0.494	6.808	6.493	7.179
<0.25	1.5-3.0	2056	0.198	0.191	0.204	2.771	2.616	2.924
<0.25	3.0-5.0	915	0.088	0.083	0.092	1.232	1.142	1.322
<0.25	5.0-15.0	3212	0.069	0.066	0.072	0.968	0.922	1.015
<0.25	15.0-40.0	1750	0.019	0.018	0.020	0.262	0.246	0.278
<0.25	>40.0	424	0.004	0.004	0.005	0.063	0.056	0.069
0.25-1.0	<1.5	121	0.012	0.010	0.013	0.162	0.138	0.186
0.25-1.0	1.5-3.0	256	0.024	0.022	0.027	0.343	0.309	0.381
0.25-1.0	3.0-5.0	240	0.023	0.021	0.026	0.324	0.288	0.364
0.25-1.0	5.0-15.0	1355	0.029	0.027	0.031	0.406	0.390	0.420
0.25-1.0	15.0-40.0	1016	0.009	0.008	0.009	0.121	0.113	0.130
0.25-1.0	>40.0	455	0.004	0.003	0.004	0.054	0.048	0.061
1.0-3.0	1.5-3.0	16	0.002	0.001	0.002	0.022	0.013	0.031
1.0-3.0	3.0-5.0	32	0.003	0.002	0.004	0.043	0.031	0.056
1.0-3.0	5.0-15.0	679	0.017	0.015	0.018	0.231	0.218	0.244
1.0-3.0	15.0-40.0	608	0.006	0.005	0.007	0.085	0.078	0.092
1.0-3.0	>40.0	186	0.001	0.001	0.002	0.020	0.016	0.024
> 3.0	5.0-15.0	98	0.003	0.002	0.003	0.035	0.029	0.041
> 3.0	15.0-40.0	246	0.003	0.002	0.003	0.036	0.031	0.040
> 3.0	>40.0	98	0.001	0.001	0.001	0.012	0.009	0.015

A comparison of zone-specific PCM adjustment factors by diameter and length category is presented in Table 4. While many of the bivariate diameter/length cells show similar PCM adjustment factors for the different zones, some potentially important differences are noted. Some zones demonstrated a greater preponderance of short, thin fibers whereas others demonstrated longer-thinner fibers (Table 4), which could substantially alter cumulative fiber exposure estimates for workers included in the mortality analyses.

Table 5 provides an example using the PCM adjustment factors in Table 4 to generate estimated mean exposures to long, thin fibers (< 0.25 µm in diameter and > 5 µm in length and not counted by PCM). This example is for UJC-A (General Area Personnel) in calendar year 1965 by exposure zone. The PCM adjustment factors for fibers < 0.25 µm in diameter and > 5 µm in length (Table 4) were multiplied by the mean PCM concentrations in each exposure zone from Dement et al. [26] to estimate the TEM concentration of long, thin fibers. This example shows that PCM adjustment factors for long, thin fibers vary substantially by textile department, with smaller factors for initial

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textile operations (e.g. fiber preparation and carding). Should exposures to these longer and thinner fibers be more predictive of disease risks, Table 5 demonstrates the potential for considerable exposure misclassification based on PCM exposure estimates.

TABLE 4

COMPARISON OF PCM ADJUSTMENT FACTORS ($F_{ijz}/FPCM_i$)
BY ZONE FOR BIVARIATE SIZE DISTRIBUTIONS

Fiber Diameter Category 'j' (μm)	Fiber Length Category 'z' (μm)	Zone1	Zone 2	Zone 3	Zone 4	Zone 5	Zone 6	Zone 7	Zone 8	Zone 9	Zone 10	Overall Plant
<0.25	<1.5	3.764	5.089	8.532	5.038	6.726	14.578	4.422	9.895	9.473	30.489	6.808
<0.25	1.5-3.0	2.695	2.508	3.011	2.423	4.407	3.774	1.962	2.972	3.032	8.181	2.771
<0.25	3.0-5.0	1.237	1.202	1.210	1.250	1.528	1.978	1.021	1.152	1.164	3.056	1.232
<0.25	5.0-15.0	0.788	0.973	0.848	0.986	0.972	1.666	0.858	1.005	1.254	1.878	0.968
<0.25	15.0-40.0	0.197	0.155	0.364	0.255	0.291	0.421	0.227	0.277	0.354	0.269	0.262
<0.25	>40.0	0.039	0.027	0.102	0.085	0.055	0.084	0.047	0.055	0.079	0.000	0.063
0.25-1.0	<1.5	0.130	0.241	0.198	0.083	0.306	0.055	0.151	0.199	0.110	1.198	0.162
0.25-1.0	1.5-3.0	0.420	0.617	0.343	0.192	0.443	0.164	0.251	0.282	0.332	0.979	0.343
0.25-1.0	3.0-5.0	0.350	0.436	0.371	0.295	0.392	0.187	0.285	0.251	0.317	0.984	0.324
0.25-1.0	5.0-15.0	0.445	0.428	0.351	0.390	0.406	0.377	0.348	0.482	0.469	0.359	0.406
0.25-1.0	15.0-40.0	0.094	0.083	0.145	0.132	0.129	0.152	0.107	0.149	0.111	0.409	0.121
0.25-1.0	>40.0	0.027	0.018	0.089	0.072	0.077	0.118	0.052	0.046	0.052	0.082	0.054
1.0-3.0	1.5-3.0	0.019	0.016	0.015	0.016	0.069	0.037	0.036	0.000	0.078	0.000	0.022
1.0-3.0	3.0-5.0	0.019	0.120	0.050	0.000	0.097	0.000	0.061	0.019	0.065	0.000	0.043
1.0-3.0	5.0-15.0	0.261	0.313	0.207	0.247	0.190	0.189	0.252	0.170	0.204	0.107	0.231
1.0-3.0	15.0-40.0	0.071	0.079	0.104	0.075	0.106	0.100	0.115	0.073	0.074	0.000	0.085
1.0-3.0	>40.0	0.012	0.010	0.020	0.026	0.023	0.015	0.018	0.020	0.035	0.000	0.020
> 3.0	5.0-15.0	0.048	0.040	0.043	0.038	0.019	0.000	0.035	0.035	0.023	0.085	0.035
> 3.0	15.0-40.0	0.043	0.036	0.046	0.027	0.045	0.000	0.063	0.022	0.022	0.000	0.036
> 3.0	>40.0	0.007	0.010	0.020	0.012	0.007	0.052	0.010	0.004	0.010	0.000	0.012

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TABLE 5

TEM SIZE SPECIFIC JEM EXAMPLE

ESTIMATED TEM CONCENTRATIONS OF LONG AND THIN FIBERS

UBC-A (GENERAL AREA PERSONNEL) IN 1965 BY EXPOSURE ZONE

Exposure Zone	Plant Department Associated with Exposure Zone	Mean PCM Exposure (fibers > 5 µm/cc)	PCM Adjustment Factor	Mean TEM Exposure (fibers < 0.25 µm in diameter and > 5 µm in length /cc)
1	Preparation	5.8	1.02	5.92
2	Carding	2.4	1.15	2.76
3	Ring Spinning	8.2	1.31	10.74
4	Mule Spinning	6.3	1.33	8.38
5	Foster Winding	4.2	1.32	5.54
6	Twisting	5.4	2.17	11.72
7	Universal Winding	4.1	1.13	4.63
8	Heavy Weaving	2.6	1.34	3.48
9	Light Weaving	2.7	1.69	4.56
10	Finishing Operations	0.2	2.15	0.43

In addition to these estimates of fiber number concentrations, surface area conversion factors (not shown) were used to derive approximate surface area exposure measurements, expressed as μm^2/cc, based on the same fiber size categories shown in Tables 3 and 4, for comparison of exposure metrics in an epidemiological study of this textile cohort[37].

DISCUSSION

Results of current TEM analyses are consistent with prior TEM studies of samples from this plant [8] [9], demonstrating a preponderance of short fibers in airborne aerosols. The TEM fiber size data, combined with the prior PCM fiber concentration estimates by zone, job and time period, provide the ability to define new metrics based on single bivariate size categories or any combination of size categories. The new JEM provides unique data for the study of cancer and non-cancer endpoints among the Charleston cohort and for comparisons with other plants and facilities. Strengths of the data include use of multiple TEM samples (range 3-11) for each exposure zone with additional efforts in the TEM analyses to better capture the entire fiber size spectrum, including fibers as thin as <0.25 µm in diameter and as long as > 40µm. A limitation is the unavailability of samples and resources to further study differences by job groups within each zone. However, based on our *a priori* knowledge of plant processes, jobs, and fiber characteristics within each zone, the assumption that jobs within a given exposure zone share similar airborne fiber size characteristics appears justified [8][9][26].

Given that the samples for TEM analyses do not cover the entire period for which PCM estimates are available, only a single point estimate for the PCM adjustment factors could be developed for each exposure zone. The implicit assumption is stability of the airborne fiber size distribution over calendar time within each exposure zone (while changes in the airborne fiber concentration over time in each exposure zone were based on industrial hygiene sampling data over time). The process of making asbestos textiles at this plant changed relatively little over the study period, both with regard to the sources of asbestos fiber used and processing equipment. Additionally, engineering controls such as local exhaust ventilation were implemented in this plant on a large scale starting before 1940 [38]; therefore, potential effects of ventilation on airborne fiber size characteristics should be minimized. Quinn et al. [24] demonstrated that bulk material factors for fibrous glass are important determinants of the airborne fiber size distribution, supporting the assumption that similar production processes applied to similar bulk fibrous material are likely to produce similar airborne fiber size distributions. Our assumption of stability of airborne fiber characteristics within a given plant operation over calendar time therefore seems reasonable and appropriate; however, we cannot completely rule out some changes in airborne fiber characteristics over time.

Our results have significant implications for epidemiological studies that seek to estimate fiber exposure-response relationships. While PCM exposure estimates provide data useful for risk assessments, the PCM method is relatively insensitive to differences in airborne fiber characteristics across and within industries and does not allow for analyses of fiber size-specific risks. Our aim is to use methods developed by this study in conjunction with ongoing epidemiological studies to better assess risks by fiber size for chrysotile [37].

CONCLUSION

While animal studies have suggested that longer and thinner fibers are more biologically active in the production of disease, few human data exist to support or refute these findings. Occupational cohorts are exposed to a wide range of airborne asbestos fibers, with the vast majority being shorter than 5 µm in length. While asbestos textile operations typically used grades of chrysotile with longer fiber lengths, the resulting aerosol to which workers were exposed was primarily comprised of short fibers. The fiber size distributions and the PCM adjustment factors were shown to vary considerably across plant operations. The methods used in this study for developing the fiber-size specific JEM are applicable in other situations where TEM data or archived samples may be available to generate bivariate size distributions and to study the role of fiber dimension in predicting asbestos-related lung diseases.

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COMPETING INTEREST

The authors have no competing interests associated with this research and manuscript.

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REFERENCES

1. Stanton M, Layard M, Tegeris A, Miller E, May M, Morgan E. Relation of Particle Dimension to Carcinogenicity in Amphibole Asbestos and Other Fibrous Minerals. J Nat Cancer Inst 1981;67(5):965-975.
2. Pott F. Problems in defining carcinogenic fibres. Ann Occup Hyg 1987;31:799–802.
3. Davis JM, Jones AD. Comparisons of the pathogenicity of long and short fibres of chrysotile asbestos in rats. Br J Exp Pathol 1988;69(5):717-37.
4. Lippman M. Effects of fiber characteristics on lung deposition, retention, and disease. Environ Health Perspect 1990;88:311–317.
5. Dement JM, Wallingford KM. Comparison of phase contrast and electron microscopic methods for evaluation of occupational asbestos exposures. Applied Occ Env Hyg 1990;5:242-247.
6. Gibbs GW, Hwang CY. Dimension of Airborne Asbestos Fibres. In Biological Effects of Mineral Fibers. J.C. Wagner, Editor: IARC Scientific Publications No. 30. 1980 Lyon, France 1980:69-77.
7. Dement JM, Harris RL. Estimates of Pulmonary and Gastrointestinal Deposition for Occupational Fiber Exposures, DHEW-NIOSH Publication No. 79-135, 1979.
8. Dement JM. Estimation of Dose and Evaluation of Dose-Response in a Retrospective Cohort Mortality Study of Chrysotile Asbestos Textile Workers. Doctoral Dissertation, University of North Carolina at Chapel Hill, 1980.
9. Dement JM, Brown DP, Okun A. Follow-up Study of Chrysotile Asbestos Textile Workers: Cohort Mortality and Case-Control Analyses. Amer J Ind Med 1994;26(4):431-47.
10. Hein MJ, Stayner LT, Lehman E, Dement JM. Follow-up study of chrysotile asbestos textile workers: Cohort mortality and exposure-response. Occup Environ Med. 2007;64:616-625.
11. Greenburg L, Bloomfield JJ. Dust Sampling Apparatus Used by the United States Public Health Service. Public Health Reports. 1932;47:654-675.
12. Holmes S. Developments in Dust Sampling and Counting Techniques in the Asbestos Industry. Ann NY Acad Sci 1964;132:288-297.
13. Addingley CG. Dust Measurement and Monitoring in the Asbestos Industry. Ann NY Acad Sci 1964;132:298-305.
14. Roach SA. Measurement of Airborne Asbestos Dust by Instruments Measuring Different Parameters. Ann NY Acad Sci 1964;132:306-315.
15. Lynch JR, Ayer HE. Measurement of dust exposure in the asbestos textile industry. Amer Ind Hyg Assoc J 1966;27:431-347.
16. Pott F, Huth F, Friedrichs K. Tumorgenic Effect of Fibrous Dust in Experimental Animals. Env Hlth Persp 1974;9:313-315.
17. Stanton MF, Wrench C. Mechanisms of Mesothelioma Induction with Asbestos and Fibrous Glass. J Natl Cancer Inst;1972;48:797-821.
18. Berman DW. Crump KS. Chatfield EJ. Davis JM. Jones AD. The sizes, shapes, and mineralogy of asbestos structures that induce lung tumors or mesothelioma in AF/HAN rats following inhalation. Risk Analysis 1996;15(2):181-95.
19. Lippmann M. Asbestos exposure indices. Environmental Research. 1988;46(1):86-106.
20. Berman DW, Crump KS. Technical Support Document for a Protocol to Assess Asbestos-Related Risk. Final Draft, October 2003. Prepared for: Office of Solid Waste and Emergency Response U.S. Environmental Protection Agency Washington, DC. EPA # 9345.4-06, 2003.

21. Raabe OG, Al-Bayati MA, Teague SV, Rasolt A. Regional deposition of inhaled monodisperse coarse and fine aerosol particles in small laboratory animals. Ann Occup Hyg 1988;32(Supple 1):653-63.

22. Asgharian B, Yu CP. Deposition of fibers in the rat lung. J Aerosol Sci 1989;20(3):355-366.

23. Quinn MM. Smith TJ. Eisen EA. Wegman DH. Ellenbecker MJ. Implications of different fiber measures for epidemiologic studies of man-made vitreous fibers. American Journal of Industrial Medicine. 2000;38(2):132-139.

24. Quinn MM, Smith TJ, Schneider T, Eisen EA, Wegman DW. Determinants of Airborne Fiber Size in the Glass Fiber Manufacturing Industry. Journal of Occupational and Environmental Hygiene. J Occup Enviro Hyg 2005;2:19-28.

25. Dement JM, Harris RL, Symons MJ, Shy CM. Estimates of Dose-Response for Respiratory Cancer Among Chrysotile Asbestos Textile Workers. Ann. Occup. Hyg., 1981;26(1-4):869-887.

26. Dement JM, Harris RL, Symons MJ, Shy, CM. Exposures and mortality among chrysotile asbestos workers. Part I: Exposure Estimates. Am J Ind Med 1983;4:399-419.

27. ISO. Ambient Air—Determination of Asbestos Fibres – Direct Transfer Electron Microscopy Method. ISO 10312, International Standards Organization, 1995.

28. National Institute for Occupational Safety and Health (NIOSH). Method for Determination of Asbestos in Air Using Transmission Electron Microscopy. NIOSH Method 7402. NIOSH, Cincinnati, Ohio, U.S.A., 1986.

29. Yamate G, Agarwal SC, Gibbons RD. Methodology for the Measurement of Airborne Asbestos by Electron Microscopy. U.S. EPA Report No. 68-02-3266. U.S. Environmental Protection Agency, Washington, D.C., U.S.A, 1984

30. U.S. Environmental Protection Agency. Asbestos Hazard Emergency Response Act: Asbestos-Containing Materials in Schools. Final Rule and Notice (Appendix A: AHERA Method). Federal Register, 40 CFR 763, Vol. 52, No. 2, pp. 41826-41903, October 1987.

31. NIOSH. Protocol for TEM Analysis of Chrysotile Asbestos: Adaptation of ISO Method for quality and cost-effective analysis of archival samples from Charleston, South Carolina textile plant by E. Kuempel, J. Dement, A. Ristich, J. Bena, R. Zumwalde. National Institute for Occupational Safety and Health, Cincinnati, Ohio, April 8, 2004.

32. SAS Institute, Inc. The SAS system, Version 8.2. Cary, NC: SAS Institute, Inc. 1999.

33. Timbrell V. Deposition and retention of fibres in the human lung. Ann Occup Hyg 1982;26(1-4):347-369.

34. Baron PA. Application of the thoracic sampling definition to fiber measurement. Am Indust Hyg Assoc J 1996;57:820-824.

35. Blake T, Castranova V, Schwegler-Berry D, Baron P, Deye GJ, Li C, Jones W. Effect of fiber length on glass microfiber cytotoxicity. J Toxicol Environ Health A. 1998 54(4):243-259.

36. Mooney CZ, Duval RD. Bootstrapping: A Nonparametric Approach to Statistical Inference (Sage University Paper series on Quantitative Applications in the Social Sciences, 07-095). Newbury Park, CA, 1993.

37. Stayner LT, Kuempel E, Gilbert S, Hein M, Dement, J. An epidemiologic study of the role of asbestos fiber dimensions in determining respiratory disease risk in exposed workers (Submitted to OEM)

38. Page RT, Bloomfield JJ. A Study of Dust Control Methods in an Asbestos Fabricating Plant. Public Health Reports. 1937 52(48):1713-1727.

FIGURE LEGENDS
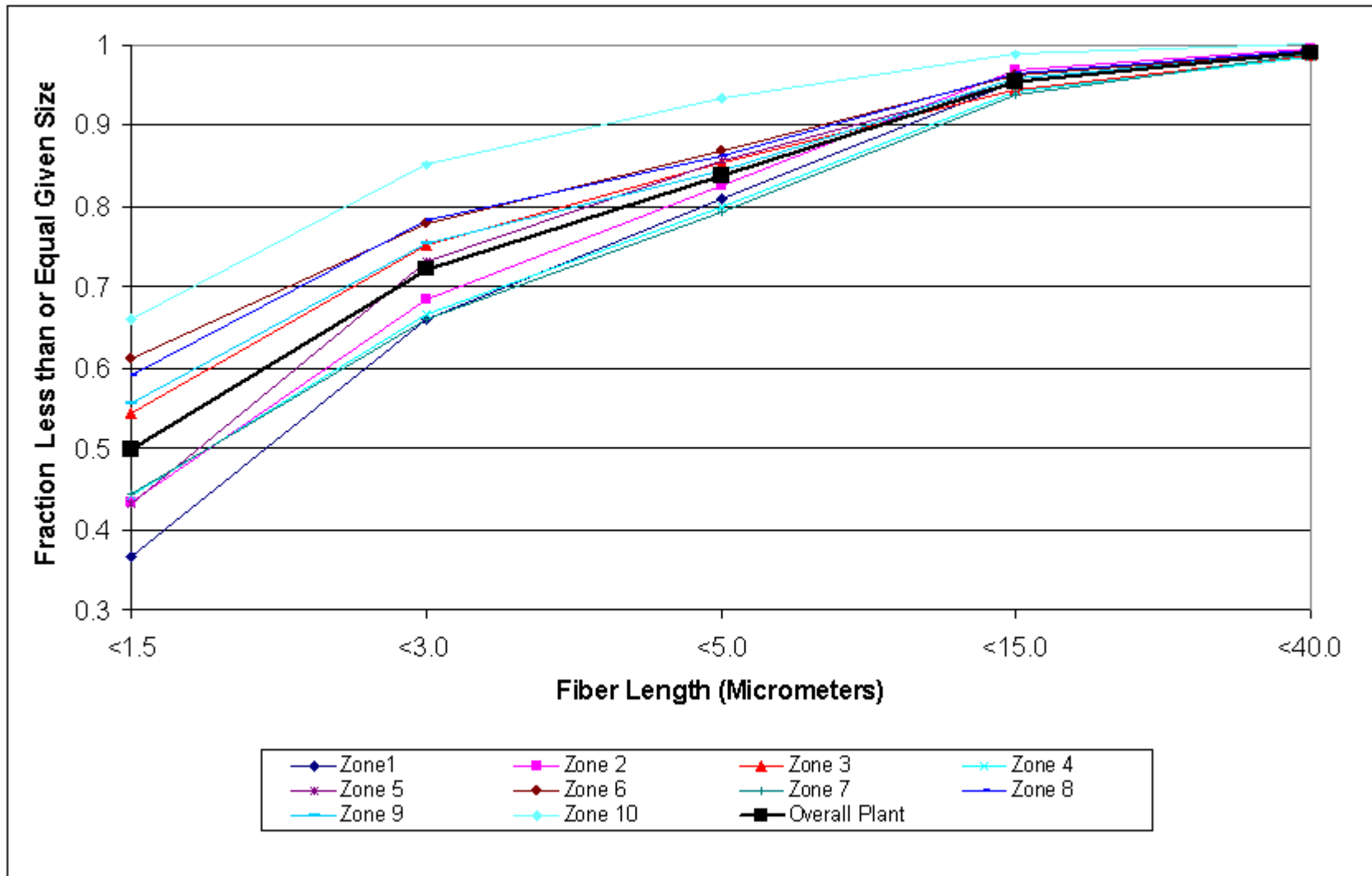FIGURE 1: TEM CUMULATIVE FIBER LENGTH DISTRUBUTION BY PLANT EXPOSURE ZONE

FIGURE 2: TEM CUMULATIVE FIBER DIAMETER DISTRUBUTION BY PLANT EXPOSURE ZONE

FIGURE 1

TEM CUMULATIVE FIBER LENGTH DISTRUBUTION BY PLANT EXPOSURE ZONE

FIGURE 2

TEM CUMULATIVE FIBER DIAMETER DISTRUBUTION BY PLANT EXPOSURE ZONE