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Developing a company-specific job exposure matrix for the Asbest Chrysotile Cohort Study

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ABSTRACT

Objectives Exposure assessment for retrospective industrial cohorts are often hampered by limited availability of historical measurements. This study describes the development of company-specific job-exposure matrices (JEMs) based on measurements collected over five decades for a cohort study of 35 837 workers (Asbest Chrysotile Cohort Study) in the Russian Federation to estimate their cumulative exposure to chrysotile containing dust and fibres.

Methods Almost 100 000 recorded stationary dust measurements were available from 1951-2001 (factories) and 1964–2001 (mine). Linear mixed models were used to extrapolate for years where measurements were not available or missing. Fibre concentrations were estimated using conversion factors based on side-by-side comparisons. Dust and fibre JEMs were developed and exposures were allocated by linking them to individual workers' detailed occupational histories.

Results The cohort covered a total of 515 355 employment-years from 1930 to 2010. Of these individuals, 15% worked in jobs not considered professionally exposed to chrysotile. The median cumulative dust exposure was 26 mg/m^3 years for the entire cohort and 37.2 mg/m^3 years for those professionally exposed. Median cumulative fibre exposure was 16.4 fibre/cm^3 years for the entire cohort and 23.4 fibre/cm^3 years for those professionally exposed. Cumulative exposure was highly dependent on birth cohort and gender. Of those professionally exposed, women had higher cumulative exposures than men as they were more often employed in factories with higher exposure concentrations rather than in the mine.

Conclusions Unique company-specific JEMs were derived using a rich measurement database that overlapped with most employment-years of cohort members and will enable estimation of quantitative exposure–response.

Key messages

What is already known about this subject?

► Occupational exposure assessments in epidemiological studies aim to obtain accurate, precise and biologically relevant estimates, which can be meaningfully applied to assess an individual's exposure. In retrospective cohort studies limited exposure information over time can hamper this process. Most published chrysotile cohort studies have used a variety of methods to determine exposure, with limited data for relatively small industrial cohorts.

What are the new findings?

► The exposure estimates derived are the most well-informed metrics available for a quantitative epidemiological risk analysis for occupational exposure to dust containing chrysotile asbestos. They show that workers employed in earlier years had considerable higher cumulative exposures and exposed women appeared to have considerably higher cumulative exposure than men mainly due to working in areas with higher exposures. Additionally, our analyses showed cumulative and average exposure intensity dust and fibre exposures to be strongly correlated (>0.70).

How might this impact on policy or clinical practice in the foreseeable future?

► This study has outlined the development of comprehensive, company-specific job-exposure matrices that will be applied in exposure–response analyses between chrysotile dust and fibre concentrations and cancer mortality within the Asbest Chrysotile Cohort Study. Given the size, make-up and exposure history of the cohort deriving sex-specific risk estimates will be possible.

INTRODUCTION

Occupational exposure assessments in epidemiological studies aim to obtain accurate, precise and biologically relevant estimates which can be meaningfully applied to assess an individual's exposure. Limited historical exposure information can hamper this process. Gold-standard exposure measurements come from detailed monitoring but are generally only available in cross-sectional or prospective studies. Therefore, retrospective, historical studies rely on alternative techniques including qualitative measures, and quantitative estimates derived from expert judgement, job-exposure matrices (JEMs), self-reported exposure or a combination.[1 2] Even when measurements have been collected historically, complete coverage is not common[3] and, as a result, some level of estimation or modelling is required to extrapolate exposure for years without measurements.[1 2 4–6]

The Asbest Chrysotile Cohort Study is a historic cohort study of workers employed in the chrysotile enrichment factories and mine of the Joint Stock Company (JSC) Uralasbest in Asbest, Southern Urals, the Russian Federation, which commenced in 2010.[7 8] As a company-specific cohort study, the Asbest Chrysotile Cohort Study requires a detailed company-specific JEM to permit the allocation of occupational exposure to chrysotile containing dust and fibres based on detailed occupational histories. From the 1950s, JSC Uralasbest systematically collected almost 100 000 stationary dust measurements across the various factories and the mine. The aim of this paper is to outline the development of company-specific JEMs in order to estimate dust and fibre exposures for workers and to illustrate estimated cumulative exposure to chrysotile containing dust and fibres within the cohort.

METHODS

Details of the Asbest Chrysotile Cohort Study have previously been described.[7 8] In brief, the cohort comprised 35 837 workers eligible for the study who worked for at least 1 year between 1975 and 2010 in factories and mine. The start year of 1975 was selected as the starting employment year as early, pilot data investigations showed that follow-up for mortality and migration would be incomplete and of lower quality before 1975 in this area of Russia.[7] Using personal and occupation-related information extracted from company records, individual detailed occupational histories were recorded. Work locations were grouped into two areas. First, the mine and external rail group which involved the extraction of ore and its transportation. Second, the factories group where ore was broken down, enriched and refined, through a process of crushing and sorting, to consumer products.

JSC Uralasbest was established in 1896 and is still operational, largely focusing on the production of 50 kg packages of chrysotile, graded for use in textiles, pipes, slate and fillers. Over the study period, seven factories (numbered 0–6) as well as several mines, later combined into one, were in operation and exposure was measured by the Central Laboratory (online supplemental table 1). At its peak of production in the 1970s and 1980s, there were up to five factories operating at one time. From 1886 to 2001, over 4.5 billion tons of ore were mined and 43 million tons of chrysotile were produced. The currently reported production capacity of JSC Uralasbest is 300 thousand tons of chrysotile per year from 30 million tons of ore, with a combined mine and one factory in operation (factory 6).[9–11]

Exposure monitoring and dust estimates

At JSC Uralasbest, dust concentrations were measured and recorded systematically starting in 1951 for the factories and 1964 for the mine and external rail. Dust monitoring continues to the present day. Due to a flood at JSC Uralasbest, all dust concentration records for the factories were destroyed for the years 1956–1958.

The method of collection and time trends in dust concentrations have been described previously.[12] The measurements were taken at sampling points, located in areas corresponding to the breathing zone of workers or as close as possible,[12] either once per month or every 10 days in the factories, and approximately once every 3 months in the mine.[12]

The Central Laboratory used stationary sampling techniques and reported measurements of all operations by sampling point, a fixed point in a factory or mine representing a physical area where work was conducted. A comprehensive dictionary mapped the sampling points to job groups (set of job titles) and a job group code was allocated to each worker's detailed occupational history record.[12] In order to account for mobility of workers, job groups could be mapped to measurements from multiple sampling points. However, the sampling points were stationary and concentrations were not weighted for proportion of time spent around different sampling points or adjusted for variability in length of working shift. This method was used up to and including 2001 to reflect the national compliance standards for exposures in the workplace. From 2002 onwards, official reporting practices changed as the national standards were updated and JSC Uralasbest was required to report time weighed shift averages rather than measurements by sampling point. The reported time weighed shift averages were not used in this study and from 2002 onwards exposure estimates were, therefore, extrapolated to ensure consistency of exposure allocation using sampling point measurements for a total of 13% of the person-years.

Arithmetic mean monthly dust concentrations by sampling point were estimated based on available measurements per sampling point. Before an annual concentration by sampling point was derived, set criteria were applied. The criteria were that a sampling point required at least 2 monthly concentrations per year and at least 1 monthly concentration in one of two season categories, broadly defined as summer (June–September) and winter (October–May). When criteria were met, an annual average concentration per sampling point was estimated using the monthly measurements and, in the mine, a weight of 2:1 for winter versus summer (due to the long winter season) was applied. When criteria were not met, the sampling point was considered to have insufficient information and data were modelled and missing annual averages extrapolated. Sampling points were linked to a job group code using the Central Laboratory's comprehensive dictionary mapping sampling points and enable the eventual linkage to individual occupational histories. A job group for this study was a company-specific combination of job title and work location in a given time period. The sampling point annual average concentrations (mg/m^3) were used to derive a job group code annual average concentration by taking the arithmetic mean annual concentration across all sampling points linked to a given job group code.

Where data were insufficient or missing (years prior to sampling started, lost records and after 2001), linear mixed models were used to extrapolate annual arithmetic mean concentrations by job group codes using SAS V.9.3 (SAS Institute). The linear mixed models estimated the missing exposure data for the mine and each factory as a function of the year and job group code. The models included fixed effects of year of exposure and random effects for job group code. In the early years, extremely high monthly dust concentrations were recorded, and extrapolations from linear mixed models (not shown) resulted in extreme, unrealistic dust concentrations in early years prior to systematic dust monitoring. As a result, monthly dust concentrations by sampling point were capped at 100 mg/m^3, which affected only 1% of the monthly dust concentrations used in our study.

Fibre estimates

Unlike dust, fibres in the dust measurement samples were not measured on a regular basis. Therefore, exposure to chrysotile fibres had to be estimated using dust-to-fibre conversion factors described elsewhere.[13] Briefly, data from side-by-side dust and fibre measurements were collected at JSC Uralasbest in 1995, 2007 and 2013–2014 and were used to derive conversion

factors. The conversion factors were applied to the monthly dust concentrations by sampling point to derive a monthly estimated fibre concentration by sampling point. The monthly estimates were used to derive the annual estimated concentration of fibres per cubic centimetre of air (f/cm^3) by job group code by taking the arithmetic mean annual concentration across all sampling points linked to a given job group code. Where dust measurements were extrapolated, monthly conversions were not possible thus estimated fibre concentrations were derived by applying the conversion factor to the extrapolated annual dust concentrations by the job group code described above.

Exposure allocation

The annual average dust and fibre concentrations per job group formed the dust and fibre JEMs. Estimated annual average concentrations were linked to each cohort member based on the job performed in each calendar year of the occupational history and adjusted for proportion of the year the individual worked in that job, referred to as employment-years.

Exposure metrics

For each worker, cumulative dust/fibre exposure and average dust/fibre exposure intensity were then calculated. Cumulative exposure estimates were calculated by summing the annual exposure estimates over an individual's occupational history. The average annual exposure intensity was estimated by dividing cumulative exposure estimates by duration of work in exposed jobs (detailed process illustrated in online supplementary figures 1 and 2).

The correlation structure of cumulative and average intensity exposure metrics was established for the entire cohort, males and females and by birth cohort. Given the debate around using the arithmetic mean or the geometric mean to derive exposure estimates for risk analyses,[14] additional exposure metrics were derived based on geometric mean monthly dust and fibre concentrations by sampling point, mirroring the process above, and are presented along with their correlations.

RESULTS

The cumulative years worked by the 35 837 Asbest Chrysotile Cohort members were 515 355 employment-years (online supplementary table 1). Of these individuals, 15% worked in job groups recorded as not professionally exposed to chrysotile for their entire occupational history and they were assumed to have no exposure beyond background exposure. For the purposes of the analysis, they were not attributed an exposure but are reported in the findings as appropriate. Relatively more women worked in jobs without professional exposure to chrysotile (26%) compared with men (8%). The JEM for the factories was based on 91 402 dust measurements across the factories which covered 88% of the 167 509 professionally exposed employment-years (figure 1A). For the mine and external rail, there were 8100 dust measurements which covered 76% of the 227 458 professionally exposed employment-years (figure 1B).

The breakdown of the cohort by gender, birth year cohort, year of first job period and work location are shown in table 1. Men represented 62.7% of the cohort and 92% were exposed. Women represented 37.3% of the cohort and 73% were exposed. Women, however, had a slightly higher median number of employment years than men (11.9 vs 10.4). Exposed women had considerably higher median cumulative dust and fibre exposure than exposed men (respectively, 49.4 vs 31.4 mg/m^3 years and 32.9 vs 19.3 fibre/cm^3 years).

As expected, the median work duration and cumulative dust and fibre exposures decreased by birth cohort and year of first job period. By work location, workers were categorised into three groups: those who only worked in the factories, those who only worked in the mine or external rail and those who worked in both (table 1). Most of the cohort had only worked in the factories and 79% of these workers were exposed. Eighty-eight per cent of those working only in the mine or external rail and 94% of those working in both mine and factories were exposed. The median work duration was longest for those in both locations followed by factories and then mine or external rail at 13.3, 11.0 and 9.8 years, respectively.

The median cumulative dust exposure was highest for workers in the factories followed by those in both areas and then those working in the mine or external rail at 53.4, 41.4 and 25.9 mg/m^3 years, respectively. Median cumulative fibre exposures followed the same pattern at 38.0, 26.0 and 15.2 fibres/cm^3 years, respectively. Figure 2 illustrates the average dust and fibre exposure intensity of professionally exposed workers by gender. For men, the average dust exposure intensity was 3.0 mg/m^3 and average fibre exposure intensity was 1.8 fibres/cm^3. For women, the average dust exposure intensity was 4.5 mg/m^3 and average fibre exposure intensity was 3.1 fibres/cm^3.

Cumulative dust and fibre exposures by gender and work location are illustrated in figure 3. For professionally exposed men, 18% (3724) had worked in factories and they had median cumulative dust and fibre exposures of 50.3 mg/m^3 years and 35.2 fibres/cm^3 years, respectively. For those whose sole work location were the mine and external rail, the median cumulative dust and fibre exposures were lower at 24.9 mg/m^3 years and 14.8 fibres/cm^3 years, respectively (58%, 11 987 men). The remaining 4954 men had worked in both locations and their cumulative dust and fibre exposures were 36.6 mg/m^3 years and 22.9 fibres/cm^3 years, respectively.

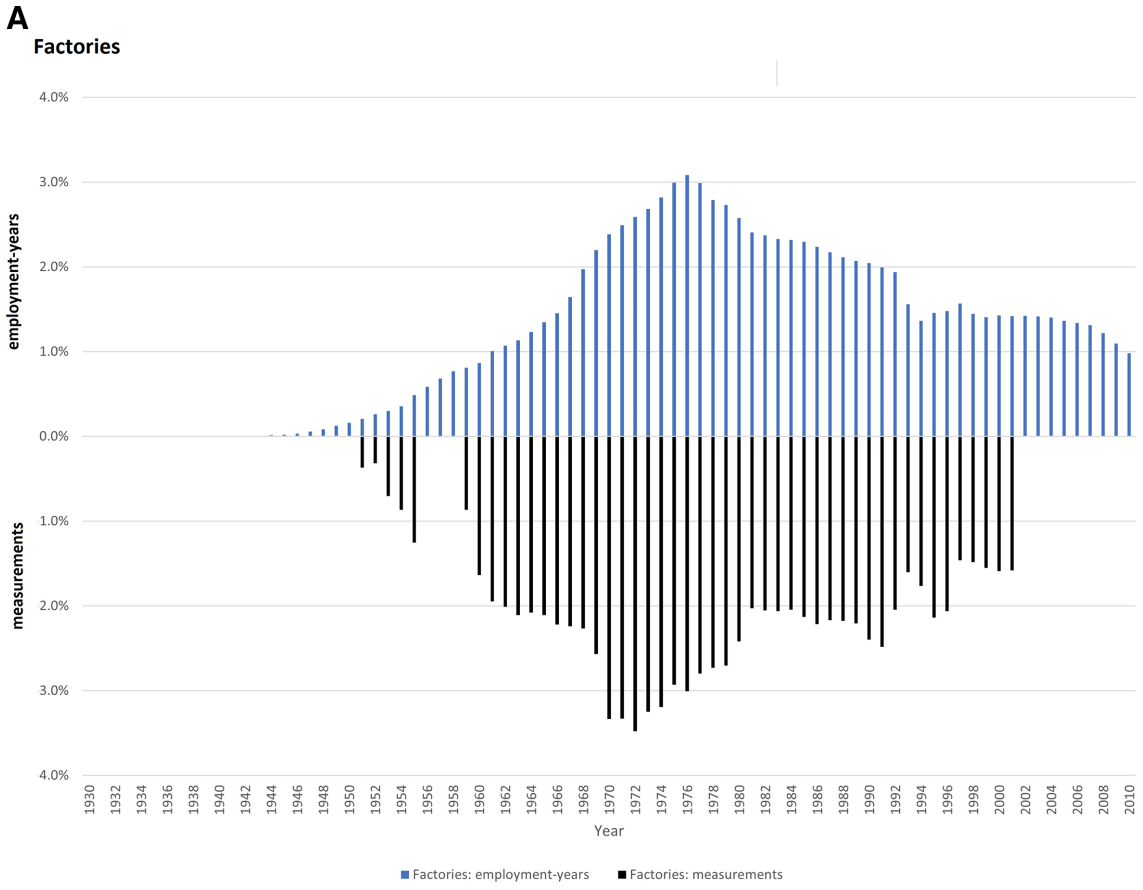
For professionally exposed women, 54% (5260) worked only in factories and they had median cumulative dust and fibre exposures of 54.8 mg/m^3 years and 39.3 fibres/cm^3 years, respectively. For those working solely in the mine and external rail, the median cumulative dust and fibre exposures were lower at 32 mg/m^3 years and 18 fibres/cm^3 years, respectively (21%, 2089 women). The remaining 2434 women had worked in both locations and their cumulative dust and fibre exposures were 50.1 mg/m^3 years and 33.6 fibres/cm^3 years, respectively.

The exposure metrics based on the geometric mean monthly dust exposure per sampling point are presented in online supplemental table 2.

The correlation structure of all derived exposure metrics is presented in online supplementary table 3. There was a strong positive correlation between cumulative dust and fibre exposure at 0.77. There was also a strong positive correlation between average dust and fibre exposure intensity at 0.70. The correlation between the estimates based on arithmetic and geometric mean concentrations per sampling point were very strong (>0.97).

DISCUSSION

The dust and fibre JEMs for the Asbest Chrysotile Cohort Study were based on almost 100 000 stationary measurements covering 5 decades which comprise the largest source of historic dust concentrations to inform a study of occupational exposure to chrysotile to our knowledge. Median cumulative dust and fibre exposure decreased over time by birth year and by year of first job, corresponding to our previous observation of decreasing dust levels with time especially in the factories.[10] Median



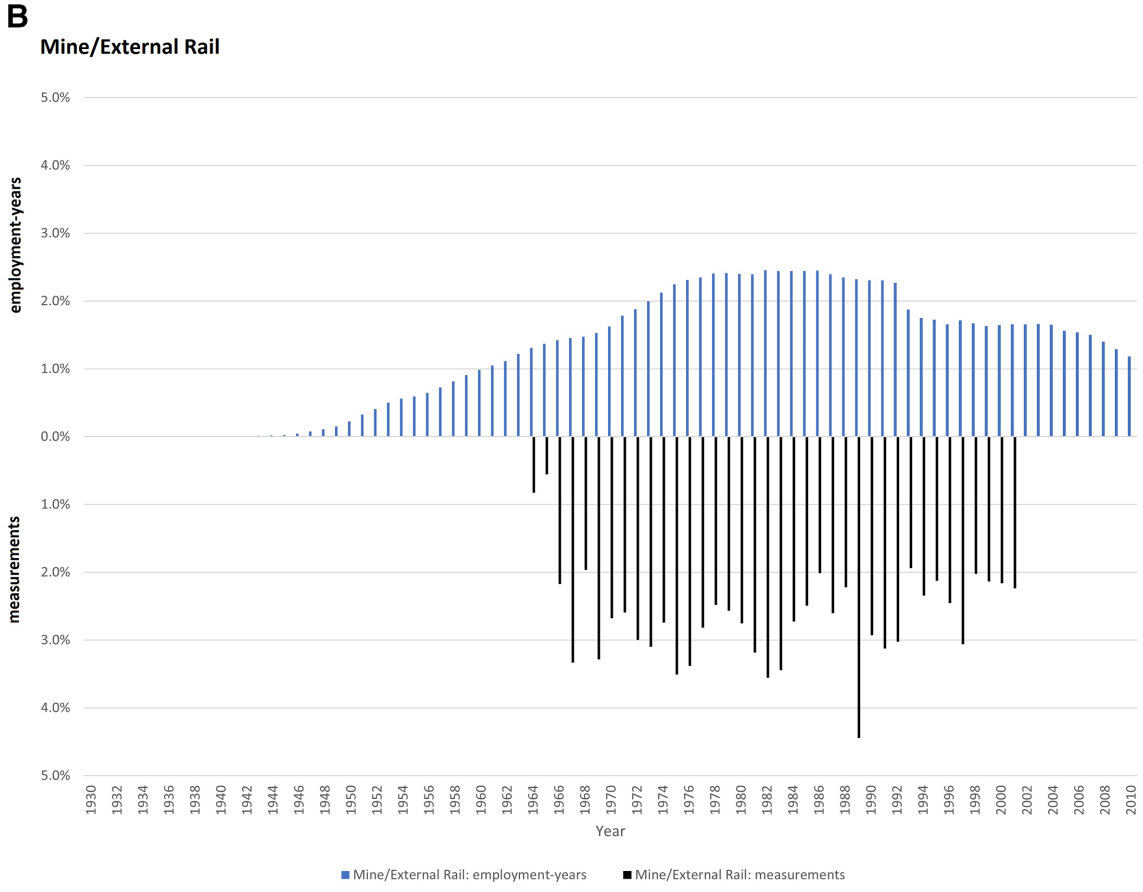


Figure 1 Distribution of employment-years of cohort members and dust measurements in the (A) factories and (B) mine and external rail.

Table 1 Key cohort characteristics and their exposure (based on arithmetic mean monthly concentration per sampling point)

			Professionally exposed					
		No of workers in cohort	No of workers in cohort professionally exposed (%)	Median work duration in professionally exposed jobs (years)	Median cumulative dust exposure (mg/m^3 years)	Median cumulative fibre exposure (fibre/cm^3 years)	Median average dust exposure intensity (mg/m^3)	Median average fibre exposure intensity (fibre/cm^3)
Gender								
Men		22 463	20 665 (92)	9.3	31.4 (0.01–1641.4)	19.3 (0.01–408.1)	3 (0.4–100)	1.8 (0.4–32.0)
Women		13 374	9783 (73)	10.9	49.4 (0.01–1184.4)	32.9 (0.01–399.8)	4.5 (0.1–100)	3.1 (0.1–43.2)
Birth cohort category								
<1930		3610	2902 (80)	18.8	88.2 (0.06–1641.4)	42 (0.01–399.8)	4.5 (1.2–100)	1.8 (0.6–43.2)
1930–1939		6226	5547 (89)	20.2	92.1 (0.04–1078.1)	50.5 (0.03–408.1)	4.6 (0.7–100.0)	2.2 (0.6–32)
1940–1949		5190	4510 (87)	13.2	54.1 (0.02–718.1)	34.4 (0.01–220.3)	3.6 (0.5–29.8)	2.1 (0.4–11.9)
1950–1959		8883	7468 (84)	8.2	27.7 (0.01–409.2)	18.1 (0.01–178.4)	3.1 (0.2–28.3)	1.9 (0.–11)
1960–1969		5979	5020 (84)	5.7	18.2 (0.01–364)	12.2 (0.01–165)	2.9 (0.1–30.1)	1.9 (0.2–9.4)
1970 on		5949	5001 (84)	4.1	13.4 (0.01–270.7)	8.9 (0.01–116.8)	3.0 (0.1–27.7)	1.9 (0.1–12)
Year of first job period								
1930–1955		3436	3268 (95)	25.1	118.5 (0.12–1641.4)	54.1 (0.01–408.1)	5.5 (1.5–100)	1.8 (1–43.2)
1955–1964		4938	4611 (93)	20	90.4 (0.07–940.4)	49.9 (0.04–296.3)	4.6 (0.7–54.6)	2.2 (0.6–16.2)
1965–1974		7219	6331 (88)	12.2	48.7 (0.02–392.2)	31.8 (0.01–220.3)	3.4 (0.5–24.3)	2.0 (0.5–10.2)
1975–1984		8857	7226 (82)	7	22.5 (0.01–409.1)	14.8 (0.01–165)	3.1 (0.1–28.3)	1.9 (0.2–10)
1985–1994		6034	4784 (79)	4.9	17.6 (0.01–328)	11.2 (0.01–140.6)	2.9 (0.1–30.1)	1.9 (0.2–11)
1995 on		5353	4228 (79)	4.1	13 (0.03–181.6)	8.5 (0.02–95.6)	2.9 (0.1–27.6)	1.6 (0.1–12)
Work location								
Factories	Total	10 180	8984 (88)	10.7	53.4 (0.04–1123.1)	38 (0.03–408.1)	5.3 (0.1–100)	3.8 (0.1–43.2)
	Men	3974	3724 (94)	10.1	50.3 (0.07–1123.1)	35.2 (0.06–408.1)	5.4 (0.2–86.4)	3.8 (0.4–20.2)
	Women	6206	5260 (85)	11	54.8 (0.04–1044.2)	39.3 (0.03–371.6)	5.1 (0.1–100)	3.7 (0.1–43.2)
Mine/ external rail	Total	17 781	14 076 (79)	9.3	25.9 (0.01–1236.6)	15.2 (0.01–96.2)	2.8 (0.4–53.5)	1.7 (0.4–2.4)
	Men	13 429	11 987 (89)	9.1	24.9 (0.01–1236.6)	14.8 (0.01–96.2)	2.8 (0.4–53.5)	1.6 (0.4–2.4)
	Women	4352	2089 (48)	10.7	32.0 (0.01–865.2)	18 (0.01–92)	3 (0.5–53.4)	1.7 (0.6–2.4)
Both	Total	7876	7388 (94)	9.7	41.4 (0.01–1641.4)	26 (0.01–399.8)	4.4 (0.1–100)	2.7 (0.2–37.3)
	Men	5060	4954 (98)	9.3	36.6 (0.07–1641.4)	22.9 (0.03–318.8)	4.2 (0.5–100)	2.5 (0.5–37)
	Women	2816	2434 (86)	10.5	50.1 (0.01–1184.4)	33.6 (0.01–399.8)	4.7 (0.1–100)	3.2 (0.2–37.3)
Total		35 837	30 448 (85)	9.9	37.2 (0.01–1641.4)	23.4 (0.01–408.1)	3.4 (0.1–100)	1.9 (0.1–43.2)

cumulative exposure was higher for women than men, driven by the majority of exposed women working in the factories where dust and fibre concentrations were higher compared with the mine and external rail. Women also had a slightly higher median work duration than men.

There was a strong correlation between dust and fibre for cumulative exposure estimates as well as average intensity of exposure to dust and fibres, partially a consequence of the derivation of fibre estimates. Both metrics will be applied in future risk analyses of chrysotile exposure and mortality.[8] Given the very strong correlation between arithmetic and geometric mean monthly average concentrations, no impact from the choice of mean in the risk estimation would be expected.[15]

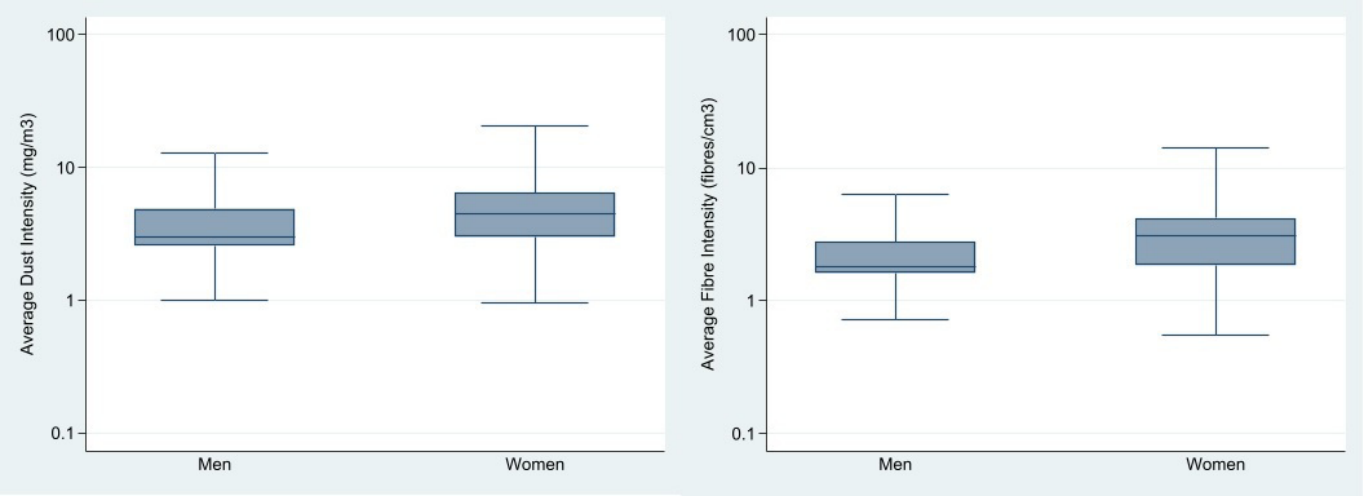


Figure 2 Average dust and fibre intensity by gender.

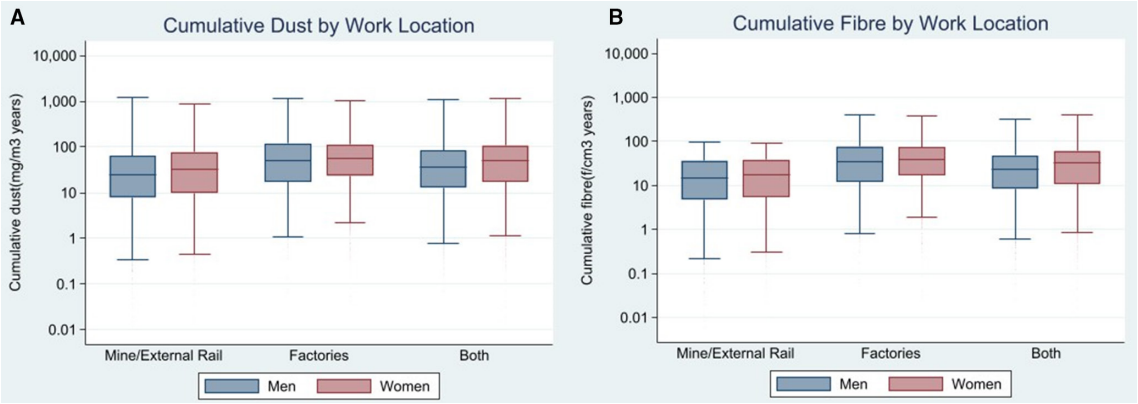


Figure 3 Cumulative dust and fibre exposure by work location and gender.

A strength of this study was the extensive, systematically collected dust measurements from which the JEM could be developed which resulted in an unprecedented coverage of 81% of person-years with actual measurements (88% and 76% in the factories and mine, respectively). This is considerably higher than previously reported for other industry based studies, for instance, three cohort studies in the petroleum industry had a person-year coverage of 9%, 10% and 46%.[3] Also, the dust measurements were collected with the same type of equipment and with the same sampling strategy over time. Only after 2001 the reporting method changed and, therefore, to ensure consistency for the years after 2001, the data from 2002 to 2010 were extrapolated (for a total of 13% of the employment-years).

Retrospective exposure assessments often require some level of estimation over the entire exposure period.[4] Detailed methodologies used for exposure estimations in other studies are not readily available in the published literature. This has limited our ability to directly compare our estimates to those from other industrial cohort studies on chrysotile exposure. There are asbestos related community-based case-control studies that face various exposure assessment derivation issues and often have to rely on expert-based and job-exposure matrix-based proxy measures in the absence of measured exposures.[16] However, recently quantitative measures have been generated for community-based case-control studies as well that resulted in convincing excess lung cancer risks at low cumulative exposure levels.[17] Thus, we have chosen to highlight the most comparable cohort studies in chrysotile mines and processing factories (including men only) and a fourth study of textile factory in South Carolina (which included women) which are compared (table 2).

The Quebec cohort of chrysotile mine workers included 10 918 men who had 425 160 person-years of follow-up to May 1992, with no reported median work duration.[18] The dust exposure data were extracted from an annual survey with midget impingers to 1966, and from 1967 onwards an estimate was used based on a 13 point scale.[18] The mean annual dust concentration for the factories decreased from the late 1940s to mid-1960s,[19] similar to the downwards trends in the Asbest Chrysotile Cohort factories and mines.[12] Cumulative dust exposure for the Quebec cohort ranged from 0 to 8000 mg/m^3 years, considerably higher than our study. In China, the Qinghai Provence Chrysotile mine cohort comprised 1539 men who worked for an average of 27.3 years.[20] The median exposure was 108.7 mg/m^3 years which was considerably higher than the median cumulative dust exposure in the Asbest Chrysotile Cohort which was 24.9 mg/m^3 years for men working in the mine who had median work duration of only 10.4 years. The Balangero mine and mill in northern Italy was active from 1917 to 1985, with a complete shutdown in 1990.[21–24] Exposure data were available based on four surveys from 1967 to 1970 and from 1975 systematic collection methods were used.[23] Cumulative fibre exposure ranged from

Table 2 Comparison of the Asbest Chrysotile Cohort with other chrysotile cohort studies

Study	N	Birth year (range)	Total person-years	Duration—median years (range)	Cumulative exposure: Dust (mg/m^3 years) Median	Dust Range	Fibre (fibre/cm3 years) Median	Fibre Range
Males								
Asbest chrysotile cohort	22 463	1891–1992	320 151	10.4 (1.0–59.5)	26.3	0–1641.4	16.3	0–408
Quebec chrysotile miners and millers[18]	10 918	1891–1920	425 160†			0.0–8000		
Qinghai provence chrysotile mine[20]	1539	1934–1957	34 736	Mean: 27.3 (21.1–33.5)	108.7	1.8–3613.5		
Balangero mine, Italy[22–24 28]	974	1877–1968	35 362	0.5–47			96.5	3–2700‡
South carolina asbestos textile plant[25]	1256	~1885–~1947	33 141	1.1 (0.1–46.8)			4.4	0.1–700
Females								
Asbest chrysotile cohort	13 374	1904–1991	195 204	11.9 (1.0–55.7)	25.1	0–1184.4	16.8	0–400
South carolina asbestos textile plant[25]	1244	~1885–~1947		0.9 (0.1–43.7)			4.2	0.2–317

NB: No other cohorts explicitly reported on professionally non-exposed workers in published materials.
* Cumulative exposures reported in this table for the Asbest Chrysotile Cohort only include cohort members that were professionally exposed and the employment-years are reported in this table.
†Person-years of follow-up to May 1992 reported for the complete cohort with no exclusions for eligibility or adjustments for analyses.
‡Derived from the published tertiles

3 to 2700 fibre/cm^3 years for a subset of 974 men with 15 760 person-years of exposure,[24] considerably higher than the men in the Asbest Chrysotile Cohort Study. In comparison to other studies, the men in our cohort have lower cumulative exposures on average which can be partially attributed to the proportion of the cohort employed in more recent time periods with lower exposure and shorter employment duration.

Although representative of a different industry, the South Carolina asbestos textile plant cohort is one of the few chrysotile studies to include women.[25] Their median work duration was approximately 1 year, and the median cumulative fibre exposure was 4.2 fibre-years for women. When compared with the South Carolina cohort, the cumulative exposure of women in the Asbest Chrysotile Cohort Study was higher. This is due to a longer employment duration for women in the Asbest Chrysotile Cohort Study despite potentially higher intensity of exposure in the asbestos textile plants of South Carolina.[25] When we compare the cumulative exposure estimates of the Asbest Chrysotile Cohort Study with those of the pooled case-control studies (including a Russian study) we see for men an almost 20 times higher exposure (19.3 vs 1.21 f/mL-years) and for women an almost 60 times higher exposure (32.9 vs 0.57 f/mL years).[17] In addition to these cohort studies, a recent developed JEM for the Baie Verte Miners' Cohort in Canada showed declining yearly average fibre concentrations from the mid-1960s to 1994[26] similar to that reported for the Asbest Chrysotile Cohort factories and mine.[13]

Our study has various limitations. The data used were monthly averages of dust concentrations. Given the strict measurement protocols used at the time, the data would not adversely impact the estimated exposure by the lack of explicit inclusion of within-day and between-day variability in exposure. Additionally, the sampling method used to collect dust concentrations used stationary samplers. Exposure based on the use of personal samplers would have been preferable, as stationary samplers may either overestimate or underestimate exposure.[27] The sampling equipment, measurement strategy, procedures and calculations are described in detail in Schonfeld *et al*.[12] Finally, there were missing exposure data and linear mixed models were required for interpolation and extrapolation. This was necessary for a total of 19% of employment-years.

Another limitation stems from converting dust concentrations to fibre which were informed by only three sets of parallel measurements relatively recently collected, as outlined in Feletto *et al*.[13] Estimated conversion factors were derived by work process unit which were consistent in the factories over time. The conversion factors appeared to be dependent on dust concentrations, that is, the higher the dust concentration the lower the conversion factor. Moreover, dust concentrations during the parallel dust/fibre measurements reached a maximum of 15 mg/m^3. To avoid underestimation of fibre concentrations at dust levels above 15 mg/m^3 occurring in earlier time periods, the estimated conversion factor used a 15 mg/m^3 cap for any dust concentration >15 mg/m^3.[13] However, the 15 mg/m^3 cap affected only 8% of the monthly concentrations used limiting the impact on epidemiological analyses. Both dust and fibre metrics will be applied in future (sensitivity) risk analyses to address the risk of bias that may arise when applying estimated fibre concentrations.

Finally, there might have been some extent of exposure misclassification especially among the 15% of the cohort whose workplaces were not systematically monitored, as was also noted in a recent study.[26] These cohort members had jobs like nursery school teachers, general cleaners and office workers who worked in locations that did not require systematic measurements to be recorded, as direct exposure in these jobs in these locations were not considered to experience relevant exposure. This practice was in line with the national regulations for monitoring occupational exposures to hazardous agents. In practice, the majority of these cohort members would have had background exposure and some might have occasionally entered areas where exposure measurements were carried out. A realistic estimate of these cohort members' exposure could not be estimated due to lack of detailed information on frequency and duration of their presence in areas with exposure and they were, therefore, considered not to be professionally exposed.

CONCLUSION

This study has outlined the development of comprehensive, company-specific JEMs to be applied in exposure-response analyses between occupational exposure to chrysotile and cancer mortality within the Asbest Chrysotile Cohort Study. The JEMs were informed by the largest reported number of measured dust concentrations, with excellent coverage of employment-years of the cohort, compared with previous studies and has enabled the estimation of annual job-specific exposure for dust and fibre. The results illustrated the high correlation of exposures derived using dust or fibre and using either arithmetic or geometric mean concentrations as input for the JEM. The exposure estimates are some of the most well-informed metrics available for quantitative risk analysis within a retrospective cohort exposed to dust containing chrysotile.

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