Supplementary material

Supplementary Table 1. Characteristics of workers in non-productive units (Asbest Chrysotile Cohort)

Characteristic	Men	Women	All
Number of workers (<i>N</i> , %)	1,797 (33)	3,590 (67)	5,387 (100)
Year of birth			
Mean	1956	1951	1952
Min–max	1891–1991	1904–1991	1891–1991
Age at start of employment (years), mean (min–max)	31 (14–87)	30 (14–75)	30 (14–87)
Age at start of employment (N, %)			
<20 years	470 (26)	922 (26)	1,392 (26)
20–29 years	579 (32)	1,366 (38)	1,945 (36)
≥30 years	748 (42)	1,302 (36)	2,050 (38)
Age at last observation (years), mean (min–max)	51 (17–97)	57 (16–99)	55 (16–99)
Duration of employment (years), mean (min–max)	8 (1–54)	9 (1–53)	9 (1–54)
Duration of employment (N, %)			
<10 years	1,363 (76)	2,417 (67)	3,780 (70)
10–29 years	358 (20)	999 (28)	1,357 (25)
≥30 years	76 (4)	174 (5)	250 (5)
Calendar year of first employment (N, %)			
Before 1970	198 (11)	653 (18)	851 (16)
1970–1999	1,171 (65)	2,681 (75)	3,852 (72)
2000 or later	428 (24)	256 (7)	684 (13)
Vital status (N, %)			
Alive	895 (50)	2,071 (58)	2,966 (55)
Deceased	676 (38)	943 (26)	1,619 (30)
Censored	226 (13)	576 (16)	802 (15)

Of 35,837 eligible workers shown in the flow diagram in Figure 1, 5 had zero follow-up time (because the date of the end of follow-up was the same as the date of becoming eligible), and an additional 5,387 workers were contractually employed by the relevant enterprises listed above but never worked in primary production activities in those enterprises. This is because those enterprises originally had their own administrative units and were also running service facilities (e.g. day-care centres, resulting in day-care workers being official employees of the mine). More recently, either these facilities became separate units in the company or the management of such service facilities was taken over from the company by Asbest town. These workplaces were not monitored for airborne dust (because exposure to airborne dust was not considered to be relevant for these workers); hence, these workers, although they had a working contract with an eligible enterprise, had no expected occupational exposure.

Therefore, the rationale for excluding these workers from the reference group of low exposure in the risk analyses was as follows: (i) although the assumed "no occupational exposure" is plausible, there is a lack of

systematic dust measurement data to prove it; (ii) some of those workers might have occasionally visited areas with exposure (e.g. a driver who usually drove administrative staff replacing a driver on sick leave who was working in the mines); (iii) as non-primary production workers, they were not included to the same extent in the regular medical surveillance of primary production workers, meaning less strict rules for admission to work for medical reasons (health status); (iv) because of less strict workplace regulations in non-primary production areas, these workers most likely had different baseline risks of many common outcomes, in particular due to less restrictive policies on known risk factors of premature death like smoking and alcohol consumption.

Supplementary Table 2. Number of workers and person-years at risk by exposure categories by cumulative exposure to dust and by cumulative exposure to fibres, by sex and combined (Asbest Chrysotile Cohort)

	Men	Women	All
	N (%)	N (%)	N (%)
Number of workers	20,662 (100)	9,783 (100)	30,445 (100)
By cumulative dust expo	osure (mg/m ³ -years) a	at the end of follow-	up (5-year lag)
≥0–20	8,597 (42)	2,839 (29)	11,436 (38)
≥20–65	6,150 (30)	3,044 (31)	9,194 (30)
≥65–150	4,251 (21)	2,581 (26)	6,832 (22)
≥150	1,664 (8)	1,319 (13)	2,983 (10)
By cumulative fibre expo	osure (fibres/cm ³ -yea	rs) at the end of foll	ow-up (5-year lag)
≥0–12	8,451 (41)	2,644 (27)	11,095 (36)
≥12–40	6,492 (31)	3,107 (32)	9,599 (32)
≥40–80	4,395 (21)	2,478 (25)	6,873 (23)
≥80	1,324 (6)	1,554 (16)	2,878 (9)
Person-years	458,883 (100)	262,429 (100)	721,312 (100)
By cumulative dust expo	osure (mg/m ³ -years) ((5-year lag)	
≥0–20	222,269 (48)	94,197 (36)	316,466 (44)
≥20–65	132,451 (29)	79,679 (30)	212,130 (29)
≥65–150	73,261 (16)	57,761 (22)	131,022 (18)
≥150	30,902 (7)	30,792 (12)	61,694 (9)
By cumulative fibre expo	osure (fibres/cm ³ -yea	ırs) (5-year lag)	
≥0–12	220,204 (48)	89,545 (34)	309,749 (43)
≥12–40	146,972 (32)	84,335 (32)	231,307 (32)
≥40–80	70,324 (15)	55,565 (21)	125,889 (17)
≥80	21,383 (5)	32,984 (13)	54,367 (8)

	Men	Women
All deaths	59.3	66.2
All cancers	63.6	63.0
Cardiovascular diseases	63.6	69.8
Respiratory diseases	59.8	65.2
Digestive diseases	57.1	59.7
External causes	47.4	53.0
Alcohol-related non-cancer diseases	48.3	53.6

Supplementary Table 3. Average age at death (in years), by cause of death and by sex^a

^a Total deaths (N=11,110)

Supplementary Table 4. Mortality rate ratios (RR) and 95% confidence intervals (CI) for categories of cumulative dust exposure and cumulative fibre exposure, by deaths from different causes and cancer sites^a, by applying lag times of 10 years and of 20 years, by sex, adjusted for age and time since last employment

	Men				Women			
Dust category		10-year lag		20-year lag		10-year lag		20-year lag
(mg/m ³ -years)			N deaths		N deaths		N deaths	
			deaths				deaths	
0 ^b	536	1.10 (0.99–1.23)		0.94 (0.87–1.01)		0.79 (0.59–1.05)		0.96 (0.82–1.14)
>0-20	2208	1.00	2097	1.00		1.00		1.00
≥20–65	2261	0.94 (0.89–1.00)	2096	0.92 (0.86–0.98)	823	1.03 (0.92–1.15)	768	0.99 (0.89–1.11)
_ ≥65–150	2079	0.90 (0.84–0.96)	1513	0.93 (0.86–1.00)	821	0.94 (0.84–1.05)	708	0.93 (0.83–1.05)
_ ≥150	1186	0.98 (0.90–1.06)	969	1.00 (0.92–1.09)	614	1.01 (0.89–1.14)	549	1.01 (0.89–1.14)
p for trend		0.11		0.83		0.77		0.96
		All cancers (ma	uin ICD	group C)		All cancers (m	ain ICD	group C)
0	44	1.20 (0.87–1.67)		1.04 (0.86–1.27)	15	0.90 (0.50–1.61)		1.03 (0.73–1.45)
>0-20	285	1.00	323	1.00	97	1.00	99	1.00
≥20–65	435	1.06 (0.91–1.24)	468	1.06 (0.91–1.22)	169	1.09 (0.85–1.41)	145	1.04 (0.81–1.35)
≥65–150	494	1.10 (0.94–1.29)	362	1.13 (0.96–1.34)	137	0.88 (0.67–1.15)	121	1.03 (0.78–1.36)
≥150	268	1.14 (0.95–1.37)	212	1.12 (0.93–1.36)	117	1.13 (0.85–1.50)	103	1.24 (0.93–1.66)
<i>p</i> for trend		0.17		0.20		0.79		0.26
<u> </u>		Lung	cancer			Lung	g cancer	
	13	1.14 (0.63–2.05)		1.03 (0.74–1.44)		1.49 (0.17–	•	4.02 (1.09–14.90)
0	25		116			13.08)		
>0-20		1.00		1.00		1.00		1.00
≥20–65		1.19 (0.92–1.55)		1.12 (0.88–1.43)		0.74 (0.28–1.95)		1.25 (0.38–4.06)
≥65–150		1.34 (1.02–1.76)		1.27 (0.97–1.67)		0.65 (0.25–1.70)		1.33 (0.41–4.31)
≥150	105	1.44 (1.06–1.95)	82	1.31 (0.97–1.79)	12	1.07 (0.42–2.75)	12	2.34 (0.75–7.38)
p for trend		0.01		0.06		0.78		0.07
		Laryngea					an cance	
^		2.46 (0.50–	3	0.47 (0.14–1.67)	1	0.61 (0.07–5.12)	5	0.81 (0.26–2.59)
0		12.18) 1.00	15	1.00	10	1.00	10	1.00
>0-20								
≥20–65		1.41 (0.61–3.29)		0.46 (0.21–1.03)		0.65 (0.26–1.58)		0.58 (0.22–1.56)
≥65–150		0.63 (0.23–1.71)		0.83 (0.37–1.88)		0.70 (0.27–1.83)		1.08 (0.39–2.95)
≥150	У	1.21 (0.44–3.35)	4	0.44 (0.14–1.39)	3	0.64 (0.21–2.01)	5	1.01 (0.32–3.20)
p for trend		0.72		0.29		0.45		0.77

	Stomach	cancer	Stomach cancer		
0	6 1.12 (0.45–2.80)	22 1.02 (0.57–1.81)	5 2.01 (0.66-6.13)	11 0.90 (0.39–2.08)	
>0-20	30 1.00	34 1.00	15 1.00	18 1.00	
≥20–65	54 1.33 (0.84–2.12)	57 1.33 (0.85–2.06)	24 1.00 (0.52–1.92)	18 0.74 (0.38–1.44)	
≥65–150	64 1.55 (0.96–2.51)	49 1.69 (1.04–2.74)	13 0.55 (0.26–1.20)	11 0.56 (0.26–1.23)	
≥150	33 1.54 (0.90–2.66)	25 1.45 (0.83–2.54)	14 0.91 (0.42–1.94)	13 0.94 (0.44–2.00)	
p for trend	0.06	0.08	0.38	0.47	
	Colorectal	cancer	Colorectal cancer		
0	3 1.59 (0.46–5.54)	12 1.54 (0.74–3.21)	1 0.44 (0.05–3.81)	6 0.72 (0.24–2.13)	
>0-20	18 1.00	20 1.00	14 1.00	13 1.00	
≥20–65	41 1.36 (0.78–2.40)	41 1.23 (0.71–2.13)	22 0.94 (0.48–1.84)	19 0.96 (0.47–1.95)	
≥65–150	43 1.09 (0.61–1.95)	35 1.23 (0.68–2.21)	22 0.83 (0.42–1.65)	24 1.27 (0.63–2.56)	
≥150	29 1.35 (0.72–2.51)	26 1.53 (0.82–2.85)	18 0.99 (0.48–2.04)	15 1.12 (0.52–2.41)	
p for trend	0.65	0.18	0.90	0.66	

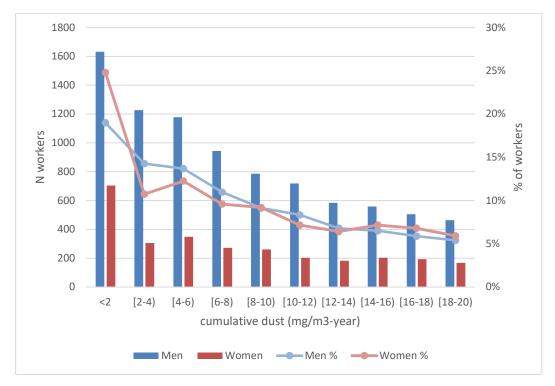
	Men			Women				
Fibre category		10-year lag		20-year lag		10-year lag		20-year lag
(f/cm ³ -years)	N		N		N		N	
	deaths	RR (CI)	deaths	RR (CI)	deaths	RR (CI)	deaths	RR (CI)
			deaths			All deaths		
0 ^b		1.10 (0.98–1.22)		0.93 (0.86–1.00)	76	0.79 (0.59–1.06)	303	0.95 (0.81–1.12)
>0-12	2256	1.00	2248	1.00	524	1.00	545	1.00
≥12–40	2621	0.94 (0.89–1.00)	2524	0.90 (0.85–0.96)	916	1.03 (0.92–1.15)	870	0.98 (0.88–1.09)
≥40–80	2064	0.86 (0.80–0.92)	1341	0.88 (0.81-0.95)	758	0.92 (0.82–1.03)	622	0.90 (0.80-1.01)
<u>≥</u> 80	793	0.97 (0.89–1.06)	562	1.02 (0.92–1.12)	566	0.95 (0.84–1.07)	500	0.98 (0.87–1.11)
p for trend		0.01		0.16		0.17		0.63
FJ	All cancers (main ICD group C)				All cancers (main ICD group C)			
0	44	1.14 (0.82–1.57)		0.97 (0.80–1.17)	15	0.91 (0.51–1.64)		1.01 (0.72 - 1.43)
>0-12		1.00		1.00		1.00		1.00
≥12–40	495	0.98 (0.85–1.14)	557	0.95 (0.83-1.09)	179	1.10 (0.86–1.42)	163	1.04 (0.81–1.33)
≥40-80	489	1.00 (0.86–1.17)	295	0.92 (0.78–1.09)	134	0.95 (0.72–1.24)	111	1.02 (0.78–1.35)
≥80	189	1.13 (0.93–1.36)	139	1.18 (0.96–1.46)	112	1.12 (0.84–1.48)	91	1.17 (0.87–1.57)
p for trend		0.34		0.57		0.75		0.51
·		Lung	cancer			Lung	g cancer	
	13	1.03 (0.57–1.85)		0.94 (0.68–1.31)	1	1.86 (0.21–		5.76 (1.38-24.01)
0						16.64)		
>0-12		1.00		1.00		1.00		1.00
≥12–40	183	1.07 (0.83–1.36)	214	1.01 (0.81–1.27)	12	1.02 (0.38–2.71)	12	2.14 (0.60–7.61)
≥40–80	187	1.17 (0.90–1.52)	109	1.03 (0.78–1.37)	9	0.74 (0.26–2.10)	9	2.00 (0.54-7.47)
≥80	75	1.36 (0.99–1.86)	52	1.32 (0.94–1.86)	13	1.49 (0.56–3.97)	11	3.36 (0.92–12.22)
p for trend		0.04		0.24		0.44		0.05

	Laryngeal	cancer ^c	Ovarian cancer		
0	2 1.65 (0.35–7.73)	3 0.45 (0.13–1.55)	1 0.59 (0.07–4.96)	5 0.69 (0.23-2.12)	
>0-12	12 1.00	17 1.00	10 1.00	12 1.00	
≥12–40	16 0.74 (0.34–1.57)	12 0.39 (0.18–0.84)	10 0.60 (0.25–1.46)	7 0.43 (0.17–1.10)	
≥40–80	9 0.41 (0.16–1.01)	10 0.71 (0.30–1.68)	9 0.72 (0.28–1.85)	10 1.09 (0.44–2.66)	
≥ 80	7 0.89 (0.34–2.37)	4 0.73 (0.23–2.28)	5 0.60 (0.19–1.84)	1 0.16 (0.02–1.32)	
p for trend	0.33	0.47	0.42	0.25	
	Stomach	cancer	Stomach	cancer	
0	6 1.05 (0.43–2.59)	22 0.96 (0.55–1.69)	5 1.79 (0.59–5.38)	11 0.84 (0.37–1.92)	
>0-12	33 1.00	39 1.00	17 1.00	20 1.00	
≥12–40	60 1.19 (0.76–1.84)	73 1.30 (0.87–1.95)	22 0.75 (0.40–1.43)	18 0.61 (0.32–1.16)	
≥40–80	70 1.55 (0.98–2.46)	40 1.40 (0.85–2.29)	15 0.60 (0.30–1.23)	14 0.72 (0.35–1.46)	
≥ 80	18 1.18 (0.64–2.17)	13 1.25 (0.64–2.42)	12 0.68 (0.32–1.46)	8 0.57 (0.24–1.34)	
p for trend	0.14	0.27	0.22	0.13	
	Colorectal	cancer	Colorectal cancer		
0	3 1.75 (0.50-6.13)	12 1.39 (0.68–2.82)	1 0.43 (0.05–3.70)	6 0.76 (0.25–2.25)	
>0-12	17 1.00	24 1.00	15 1.00	13 1.00	
≥12–40	46 1.46 (0.83–2.57)	51 1.11 (0.68–1.83)	24 0.90 (0.47–1.72)	23 1.08 (0.55–2.15)	
≥40–80	44 1.21 (0.67–2.19)	25 0.82 (0.45–1.49)	20 0.80 (0.40–1.58)	21 1.33 (0.65–2.69)	
≥80	24 1.91 (1.00-3.66)	22 1.98 (1.07–3.66)	17 0.94 (0.46–1.91)	14 1.22 (0.56–2.64)	
p for trend	0.16	0.13	0.78	0.60	

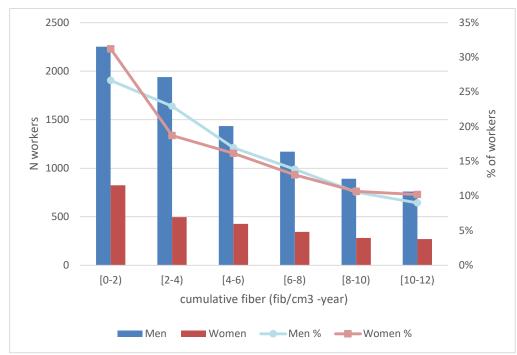
^a ICD codes for cancer sites are: lung, C33–C34; larynx, C32; ovary, C56; stomach, C16; colon and rectum, C18–C21.

^b Because the 10-year or 20-year lag time was applied, some workers had no occupational exposure to dust or fibres; as the counting of risk time started with first exposure, they are kept as a separate group and displayed only for the purpose of completeness (see Materials and Methods)

^c Only 1 case of laryngeal cancer in women; therefore, analysis for women was not carried out.



Supplementary Figure 1a. Distribution of cumulative exposure to dust within the reference category of [0,20) mg/m³-years, by sex, showing the number of workers (left y-axis) and the percentage of workers (right y-axis) in the reference category



Supplementary Figure 1b. Distribution of cumulative exposure to fibres within the reference category of [0,12) fibres/cm³-years, by sex, showing the number of workers (left y-axis) and the percentage of workers (right y-axis) in the reference category

Supplementary Information

Summary of the exposure assessment

For each cohort member and each work period, we had information on the start date and end date of the work period, the enterprise, the work unit within the enterprise, and the job group. These job groups were created based on the job title, the location of the job, and the time period, and we had 258 distinct job groups. For the exposure assessment, the occupational history was linked with a company-specific job-exposure matrix constructed from a database of more than 90,000 measurements of airborne dust taken from regular and systematic sampling across workplaces in the factories (since 1951) and the mine (since 1964) conducted mainly by the company's central laboratory (1).

For each job group, we estimated an annual average dust concentration, which was derived from measurements taken at the measurement points applicable to that job (jobs performed at multiple workplaces may have involved several measurement points). The estimated annual average dust concentration was linked to each cohort member based on the job performed in each calendar year and adjusted for the work period (proportion of the year that a worker had actually worked, according to occupational records). Thus, for each individual, cumulative exposure to airborne dust particles (in mg/m3-years) could be estimated for their entire occupational history at PJSC Uralasbest (1).

Exposure to chrysotile fibres was estimated using dust-to-fibre conversion factors derived from three series of parallel measurements of dust and fibre concentrations, conducted in 1995, 2007, and 2013–2014; these conversion factors were used to assign modelled fibre concentrations to each cohort member by job group and by calendar year (2).

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2. Feletto E, Schonfeld SJ, Kovalevskiy EV, Bukhtiyarov IV, Kashanskiy SV, Moissonnier M, et al. A comparison of parallel dust and fibre measurements of airborne chrysotile asbestos in a large mine and processing factories in the Russian Federation. Int J Hyg Environ Health. 2017; 220(5):857–68. doi: 10.1016/j.ijheh.2017.04.001.

Considerations of the healthy worker survivor bias

Within our cohort, activities related to higher exposures require good health, so the workers selected for these jobs are healthy individuals and this advantage of healthiness may have lasted throughout their working life, endorsed through the system of obligatory regular medical examinations enforced in the Russian legislation. All employees must undergo annual periodic medical examinations, and once every 5 years this examination is carried out in specialized medical institutions. If an employee's annual medical examination reveals abnormalities in health status or a change in health that is potentially related to dust exposure or may be an additional non-dust-related risk factor (e.g. obesity, frequent infectious respiratory and/or cardiovascular system problems, alcohol abuse) for developing diseases that are also possibly dust-related, then, depending on the results of the severity of symptoms from the medical examination, this employee is either recommended to stop working in places with contact with dust (but the decision remains with the employee) or is officially withdrawn from work in such conditions (although in practice this is not applied very often).

According to the pension law of the Russian legislation, the age at which retirement is allowed depends on whether the job is classified as "hazardous"; therefore, the duration of employment may be shorter in workers with higher exposure levels, and this affects the cumulative exposure measures. For example, men who have worked for more than 10 years in harmful working conditions have a right to retire at the age of 50 years (for women, after 7.5 years in harmful working conditions, the age is 45 years); the official retirement age during the study period was otherwise 60 years in men and 55 years in women. The final decision about retirement remains with the employee.

Taking all this together, as mentioned above, it is therefore possible that early symptoms of poorer health may lead to lower cumulative exposure, especially when this is a process of gradual worsening over decades, with symptoms starting during working life (e.g. for alcohol-related non-cancer diseases or infectious respiratory diseases).

Comparison with other cohort studies

Among 9,780 miners and millers in Quebec, Canada, surviving into 1936, of which 8,009 were known to have died before 1993, 38 deaths were probably from mesothelioma (1). Mortality did not vary by estimated dust level, and a relationship of increased mortality with increasing duration of employment was seen only in a group of miners with higher exposure to amphibole fibres (tremolite) (1). Based on 657 deaths from lung cancer, standardized mortality rates increased weakly with increasing estimated exposure to fibres (2).

In the Chinese cohort of 1,539 miners followed up from 1981 to 2006, with estimated fibre exposure based on conversion factors from parallel measurements, with an even higher smoking prevalence (85%) than in our study (66%) and also with a relatively young average age at death (61 years), 56 deaths from lung cancer were observed but no deaths from mesothelioma (3). Relative risks (RR) for lung cancer mortality adjusted for smoking and age at entry was 3.41 (95% confidence intervals [CI]) 1.29-8.97 for \geq 20 f-y/ml, RR 7.40 [CI 2.91-18.80] for \geq 100 f-y/ml, and RR 14.69 [CI 5.75-37.48] for \geq 450 f-y/ml when compared to study subjects exposed to <20 f-y/ml. (3). An increase in stomach-, oesophageal- and liver cancer mortality was also seen, and with an exposure -response relationship for stomach cancer (4).

Among 974 miners in Balangero, Italy, who were followed up from 1946 to 2013, there were 41 deaths from lung cancer, 8 deaths from pleural cancer, and 2 deaths from peritoneal cancer (5; slightly differing numbers due to different inclusion criteria in 6). Lung cancer mortality was increased 1.7-fold for 100–400 f/ml-years and 1.3-fold for \geq 400 f/ml-years, compared with lower estimated cumulative fibre exposure, broadly consistent with our findings (7, 8). For mesothelioma, our slope was stronger than the one observed in the Italian study but was estimated from a smaller exposure range; overall, both studies were consistent in showing significantly increased mesothelioma mortality at high cumulative exposure levels (5, 9).

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