

Continuing increase in mesothelioma mortality in Britain

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Summary

Mesothelioma is closely related to exposure to asbestos, and mesothelioma mortality can be taken as an index of past exposure to asbestos in the population. We analysed mesothelioma mortality since 1968 to assess the current state of the mesothelioma epidemic, and to predict its future course.

We found that rates of mesothelioma in men formed a clear pattern defined by age and date of birth. Rates rose steeply with age showing a very similar pattern in all five-year birth cohorts. By date of birth, rates increased from mid-1893 to mid-1948, and then fell. Relative to the 1943-48 cohort, the risk for the 1948-53 cohort is 0.79 and for the 1953-58 cohort 0.48. Despite these falls, if the age profile of rates for these cohorts follows the pattern of past cohorts, their predicted lifetime mesothelioma risks will be 1.3%, 1.0%, and 0.6%. Combining projections for all cohorts results in a peak of annual male mesothelioma deaths in about the year 2020 of between 2700 and 3300 deaths. If diagnostic trend is responsible for a 20% growth in recorded cases every 5 years—an extreme but arguable case—and if this trend has now ceased, the peak of annual male deaths will be reduced to 1300, reached around the year 2010. Analysis of occupations recorded on death certificates indicate that building workers, especially plumbers and gas fitters, carpenters and electricians are the largest high-risk group.

These data indicate that mesothelioma deaths will continue to increase for at least 15 and more likely 25 years. For the worst affected cohorts—men born in the 1940s—mesothelioma may account for around 1% of all deaths. Asbestos exposure at work in construction and building maintenance will account for a large proportion of these deaths, and it is important that such workers should be aware of the risks and take appropriate precautions.

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Introduction

Mesothelioma is almost always fatal; most patients affected die within a year of diagnosis. The majority of cases are pleural in origin, although peritoneal tumours are equally common in some groups of workers exposed to amosite (brown) asbestos. The risk is negligible up to 10 years after first asbestos exposure and very low up to 15 years, but increases thereafter as the third or higher power of time since first exposure.¹

The association of mesothelioma with asbestos was first noted in 1960,² and since 1968, the UK Health and Safety Executive has maintained a register of deaths in England, Wales, and Scotland for which mesothelioma is mentioned on the death certificate.³ Annual deaths increased from 154 in 1968 to 1009 in 1991, and increases have also occurred in other countries.⁴ The increase in rates in individuals above the age of 60 is the expected continuation of trends observed over the past 20 years, reflecting asbestos exposure when those now aged over 60 began their working lives in the early 1950s and earlier. However, there is a continuing increase in the death rate among men now aged under 50, most of whom began work in the mid 1960s or later. The increase suggests that asbestos exposure was greater around 1970 than in any previous period, and that mesothelioma rates will continue to increase as this generation ages. We describe projections of future rates calculated from these data, and discuss the possibility that occupational exposure may still be common, particularly among building workers.

Data and methods

Mesothelioma death rates in England, Wales, and Scotland for both sexes since 1968 (table 1) and male rates for men born in successive 5-year periods since 1 July 1893 were calculated from the mesothelioma register and population numbers for each year by single years of age.

The distribution of male deaths by age and year of birth (table 2) was analysed by Poisson regression, fitting the simple age and birth cohort model: annual age-specific death rate = $k_a c_b$, where k_a are predicted age-specific rates with $a=1$ for 25-29, 2 for 30-34, . . . 13 for 85-89 and c_b are birth cohort specific relative risks with $b=1$ for 1893-98, 2 for 1898-1903, . . . 13 for 1953-58. The relative risk (RR) for the 1943-48 birth cohort (c_{11}) was arbitrarily set at unity. The birth cohort RRs are thus measured relative to the 1943-48 cohort, and the k_a s are the predicted age-specific death rates for this cohort. Because the observation period is defined by calendar year of death, when the data are presented by year of birth and age at death, as in table 2, the observations for the youngest and oldest deaths for each birth cohort are incomplete. Thus for men born between mid-1913 and mid-1918 the youngest deaths during 1968-91 fall in the age group 45-49, but all these deaths are at ages 49.5 and more. The men contributing to this cell of table 2 are thus on average nearly two and a half years older than those contributing to the 45-49 age group for the 1923-28 cohort, for whom the observations in this age range are complete. The second youngest and the oldest cells for each birth cohort are also incomplete, and have mean

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Year		Age							Total
		25-34	35-44	45-54	55-64	65-74	75-84	85+	
Males									
1968-71	Obs	5	28	83	215	139	45	9	524
	Rate	0.37	2.16	6.33	17.53	18.54	16.20	19.53	8.38
1972-76	Obs	12	35	198	345	322	84	12	1008
	Rate	0.64	2.21	11.97	23.72	30.83	23.22	18.91	12.55
1977-81	Obs	7	68	265	529	562	242	18	1691
	Rate	0.36	4.21	17.04	36.31	50.96	57.53	26.82	20.66
1982-86	Obs	8	87	318	830	829	434	43	2547
	Rate	0.31	4.80	21.02	56.44	77.95	87.67	57.26	30.49
1987-91	Obs	5	107	471	1133	1341	705	82	3844
	Rate	0.24	5.57	30.29	80.84	122.34	128.39	80.73	44.02
Females									
1968-71	Obs	2	13	30	48	47	19	2	161
	Rate	0.15	1.01	2.19	3.52	4.46	3.43	1.56	2.28
1972-76	Obs	5	9	35	75	93	23	9	249
	Rate	0.27	0.58	2.06	4.64	6.64	3.10	4.72	2.76
1977-81	Obs	5	21	32	120	133	70	9	390
	Rate	0.26	1.32	2.03	7.49	9.24	8.51	4.21	4.25
1982-86	Obs	5	22	36	123	174	73	20	453
	Rate	0.26	1.22	2.37	7.77	12.73	8.04	8.04	4.86
1987-91	Obs	3	18	60	132	246	131	24	614
	Rate	0.14	0.94	3.85	8.94	18.02	13.68	7.84	6.36

Table 1: Numbers of mesotheliomas mentioned on death certificates (Obs) and death rates per million (Rate) in England, Wales, and Scotland by age and sex 1968-91

ages about 0.7 years higher and 1.3 years lower, respectively, than the mid-point of the age-group ranges. In the regression analysis, the fit to cells with incomplete observations was iteratively adjusted by log-linear interpolation to allow for their difference in mean age from the corresponding complete cells. The estimates k_a and c_b were multiplied to give predicted death-rates for each age group and birth-cohort. The fitted numbers shown in table 2 are the product of these predicted rates and the man-years in each cell. The predicted rates were then used to calculate future mesothelioma deaths in men and the lifetime (to age 90) probability of dying of mesothelioma for each birth

cohort by standard actuarial methods, assuming 1992 British male death-rates for all other causes of death in the future (figures 1 and 2).

Indirectly age-standardised occupational proportional mortality ratios (PMRs) for male mesothelioma deaths are shown in table 3. These were calculated in the standard way according to the last full-time occupation as recorded on male death certificates for ages 16 to 74 during 1979-90 (excluding 1981, when a strike by registrars made the occupational data less reliable). Complete data and a description of the occupational classification will be published separately.¹

Year of birth (relative risk c_b)	Age (death rate k_a)												
	25-29 (0.43)	30-34 (0.67)	35-39 (2.77)	40-44 (8.12)	45-49 (23.0)	50-54 (55.6)	55-59 (128)	60-64 (244)	65-69 (418)	70-74 (730)	75-79 (1103)	80-84 (1661)	85-89 (1737)
1893-1898 (0.023)									0	45	53	46	24
									0.3	36.9	59.8	49.3	21.6
1899-1903 (0.048)								0	67	120	139	140	57
								0.5	67.2	140.1	140.8	119.4	55.0
1903-1908 (0.068)							0	92	155	230	263	203	27
							0.5	77.1	174.0	235.9	244.5	206.8	31.3
1908-1913 (0.107)						2	69	191	288	392	395	81	
						0.4	72.3	190.9	279.7	386.7	393.6	94.5	
1913-1918 (0.153)					2	34	144	242	378	489	489	136	
					0.2	41.3	141.8	245.4	352.9	486.1	446.4		
1918-1923 (0.240)				1	28	96	227	432	638	204			
				0.1	33.6	113.3	245.7	429.0	610.0	194.2			
1923-1928 (0.382)			0	17	76	192	374	606	187				
			0.1	17.5	72.0	168.0	366.3	609.0	219.0				
1928-1933 (0.460)		0	7	22	81	189	413	150					
		0.0	7.3	29.6	82.2	192.8	399.0	161.1					
1933-1938 (0.634)	0	2	12	43	108	250	112						
	0.0	2.2	13.9	40.1	111.4	245.9	113.4						
1938-1943 (0.904)	4	5	18	62	160	76							
	2.3	5.2	21.1	60.9	158.3	77.2							
1943-1948 (1.000)	3	7	33	77	31								
	4.4	6.7	27.3	74.2	38.3								
1948-1953 (0.788)	4	4	19	12									
	3.3	5.0	19.2	11.5									
1953-1958 (0.479)	1	4	2										
	2.0	2.9	2.1										

Each cell shows the observed number (italicised) of mesothelioma deaths, and the fitted number derived from the birth cohort model by multiplying the population man-years (not shown) by the product of c_b and k_a (see methods). *Fitted (to age 49) and predicted (from age 50) death rates per million for 1943-1948 birth cohort. (k_a), mid-year to mid-year.

Table 2: Mesothelioma deaths in British men 1968-91, and fitted numbers based on birth cohort analysis

Results

Age and birth cohort

Close agreement between numbers of mesothelioma deaths and fitted numbers derived from the age and birth cohort analysis (table 2) shows that this model accounts well for the observed trends. Figure 1 shows the corresponding predicted lifetime probability of dying of mesothelioma for men born in different periods. The estimated lifetime risk (to age 90) increases steadily from 0.03% for men born between 1893 and 1898 to 1.3%, or about 1 in 80, for men born in 1943-48 (mid-year ranges). The estimated lifetime risks for the last two birth cohorts are 1.0% (1948-53, based on 39 deaths) and 0.6% (1953-58, based on 7 deaths), but with wide confidence intervals. Predicted numbers of mesothelioma deaths in men over the next 50 years based on these estimates are shown in figure 2. Ignoring the possibility of secular trends in under-diagnosis or over-diagnosis, these predictions are reasonably reliable up to about 2020, when over 70% of all mesothelioma deaths will still be occurring in men born before 1948. After 2020, however, the prediction will rapidly be dominated by men born after 1958 for whom no data are yet available. If their risk is negligible, the epidemic will peak at about 2700 deaths per year and will disappear rapidly after 2020. If their lifetime risk is 50% of the 1943-48 maximum, the annual total will peak at about 3300 deaths around 2020 and then fall to about 2300 deaths per year. The eventual risk is likely to lie somewhere between these limits.

Diagnostic trend

The main reservation concerning these predictions is the possibility that part of the increase in recorded death rates is an artifact of misdiagnosis. If the true rate is $k_a c_b$ for age-group, a , and birth cohort, b , an increase in recorded rates at all ages by a constant factor r from each 5-year period to the next due to a continuing increase in completeness of diagnosis (or of over-diagnosis) will mimic an epidemic with age-specific rates proportional to $r^k k_a$ and birth cohort relative risks, $r^b c_b$, suggesting a spuriously steep increase in risk, both with increasing age and in successive birth cohorts. Such a secular trend in diagnosis would be statistically indistinguishable from a real increase, but would cease as soon as reasonably complete diagnosis was achieved.

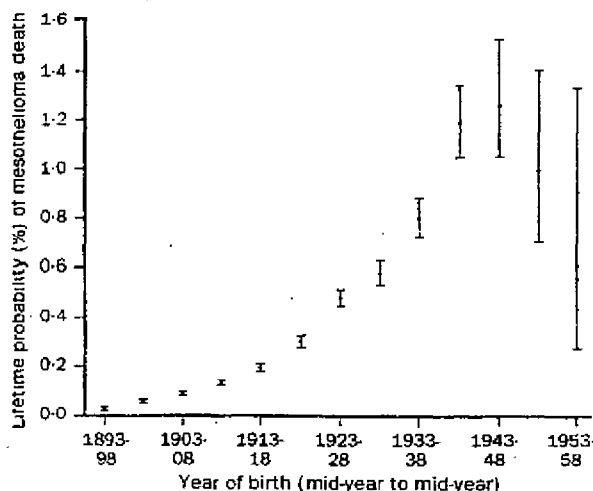


Figure 1: Predicted lifetime probability of dying from mesothelioma for British men by year of birth (95% confidence intervals)

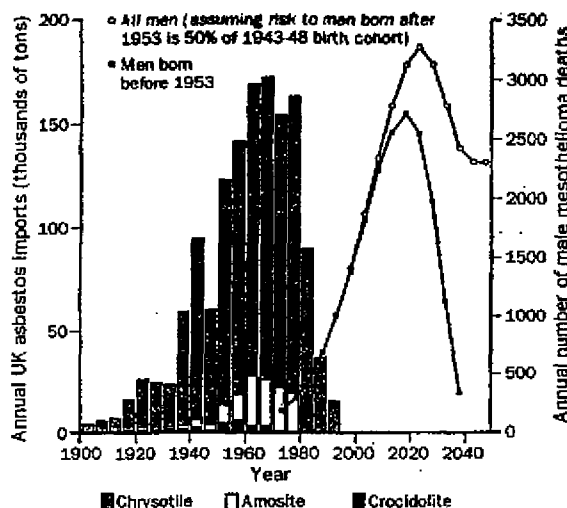


Figure 2: Predicted mesothelioma deaths in British men and UK asbestos imports

One aspect of our analysis suggests some diagnostic trend. The mesothelioma rate among USA insulation workers¹ was approximately proportional to time since first exposure raised to the power 3.2, and a similar value (3.5) was estimated for Australian crocidolite (blue) asbestos miners,⁴ but the increase with age of our predicted death rates k_a (table 2) suggests a power greater than 4. Assuming an average age at first exposure of 25, for example, the rates for ages 45-79 estimated from our simple age-cohort model are roughly proportional to (age minus 25) to the power of 4.5. Refitting the age-cohort model with the addition of a diagnostic factor of 1.2 (ie, a 20% increase in recorded rates from each five-year period to the next) produces a fit to past observations identical to that shown in table 2, but with age coefficients proportional to (age minus 25) to the power of 3.2. A diagnostic factor of around 1.2 thus brings the pattern of age coefficients more closely in line with the increases in

Job	PMR (all men=100)	Number	Percent	Cumulative percent
Metal plate workers	700.4*	110	2.5	2.5
Vehicle body builders	618.7*	35	0.8	3.2
Plumbers and gas fitters	442.8*	201	4.5	7.7
Carpenters	365.7*	258	5.7	13.5
Electricians	290.5*	161	3.6	17.0
Upholsterers	283.3†	19	0.4	17.5
Construction workers nec	255.6*	187	4.2	21.6
Boiler operators	253.9*	39	0.9	22.5
Electrical plant operators	253.5*	18	0.4	22.9
Chemical engineers & scientists	248.4*	18	0.4	23.3
Sheet metal workers	233.2*	48	1.1	24.4
Scaffolders	225.6†	11	0.2	24.6
Production fitters	216.3*	304	6.8	31.4
Professional engineers nec	210.6*	105	2.3	33.7
Plasterers	202.8*	27	0.6	34.3
Welders	202.6*	70	1.6	35.9
Managers in construction	196.8*	40	0.9	36.8
Dockers and goods porters	195.1*	69	1.5	38.3
Electrical engineers	187.0*	39	0.9	39.2
Technicians nec	171.9†	24	0.5	39.7
Buildings and handyman	164.4*	98	2.2	41.9
Laboratory technicians	164.2†	27	0.6	42.5
Draughtsmen	160.6†	28	0.6	43.1
Machine tool operators	133.0*	179	4.0	47.1
Painters and decorators	131.0†	100	2.2	49.4

* $p < 0.001$, † $p < 0.01$, ‡ $p < 0.05$. Highest 25 occupational PMRs based on 10 or more deaths.

Table 3: Proportional mortality ratios (PMR) of men aged 16-74 from mesothelioma in England and Wales 1979-80, 1982-90

risk with time since first exposure seen in other cohort studies.

Projections with these lower age coefficients, together with the assumption that no further diagnostic increases will occur after 1995, would imply that the number of male mesothelioma deaths will rise much more slowly, reaching a peak of about 1300 around the year 2010, and about 1500 per year including women.

Occupations at risk

The proportional mortality ratios (PMR) for different occupations in table 3 show the highest risk in metal-plate workers (the occupational category which includes shipyard workers) and vehicle body builders. These two occupational categories accounted for 3% of all male mesothelioma deaths. The next three highest PMRs are for plumbers and gas fitters, carpenters, and electricians, and a further six of the 25 occupational groups shown in table 3 are also in construction or related trades. These nine groups account for 1083 deaths, or 24% of the total.

Discussion

The prediction that British mesothelioma rates will continue to rise for many years is fairly secure. Whether the eventual total will be of the order of 3000 deaths per year, as the simple cohort analysis suggests, depends on several factors. Our analysis is based on death certificates on which mesothelioma is mentioned, with no systematic histological review. Misdiagnosis was certainly common in the past, particularly for peritoneal mesotheliomas; pathological review of deaths occurring among insulation workers in the USA up to 1976 increased the number of peritoneal mesotheliomas from 23 recorded on the original death certificate to 112.⁷ The corresponding figures for pleural mesothelioma were 37 by death certification and 63 after review. The UK misdiagnosis rate during the 1970s was also substantial. 38% (17/45) of mesothelioma deaths among workers in a London asbestos factory were originally attributed to other cancers.⁸ There may also have been some degree of over-diagnosis in recent years.⁹ There are, however, several qualitative arguments which suggest that diagnostic trends cannot account for a large part of the recent increase in recorded rates. First, the increase in rates from 1982-86 to 1987-91 was as great as in earlier periods. Such a striking diagnostic increase over the last decade seems unlikely. Second, mesothelioma rates in cohort studies of asbestos workers continue to rise with increasing time since first exposure. In contrast, the national mortality data suggest a roughly constant death-rate above age 55 for 1968-71 and now show a peak in the death-rate at about age 75 (table 1), a pattern characteristic of cross-sectional rates in a progressive epidemic. The strongest reason for accepting that the generation of British men born between 1940 and 1950 may have a high risk of mesothelioma is that the first 10-20 years of their working lives coincided with the peak of asbestos imports to Britain during the 1960s and 1970s (figure 2). But although improvements in diagnosis cannot entirely account for the observed increase in rates, even a small diagnostic trend could substantially affect the long-term projections. Our long-term predictions also depend on the assumption that the death-rate in men born since about 1940 will continue to increase with increasing age as sharply as in earlier generations. The relationship between age and the predicted death rate shown in table 2 arises

from men whose asbestos exposure often continued throughout their working lives. If asbestos exposure fell sharply after (say) 1980, this will not be the case for men born after 1940, because their exposure will have largely ceased by the age of 40. The rates for this and subsequent cohorts may therefore not continue to rise as steeply as in earlier generations. There is as yet no direct evidence of any change in the pattern of age dependence, but the lower rates recorded for the 1948-53 and 1953-58 birth cohorts indicate that population exposure has indeed fallen.

Irrespective of future trends and past errors of diagnosis, total asbestos-related cancer deaths in the UK must be substantially greater than the number of recorded mesothelioma deaths. As noted above, diagnostic review of deaths among asbestos workers increases the number of deaths attributed to mesothelioma, especially those originating in the peritoneum. Cohort studies of workers heavily exposed to asbestos also show an excess of lung cancer similar to the mesothelioma risk for crocidolite and greater for other types of asbestos.⁴

Since the carcinogenic effects of asbestos were widely recognised by the mid 1960s, it is surprising that the worst effects should have been experienced by the generation of men who began work after this date. The explanation is that most exposures (not the most intense, but affecting large numbers) occurred in occupational settings, particularly in the building industry, which were and still are largely unmonitored. After introduction in the UK of the 1969 Asbestos Regulations, HM Factory Inspectorate (HMTI) adopted the hygiene standard recommended by the British Occupational Hygiene Society (1968),¹⁰ which was 2 fibres/mL for chrysotile (white), amosite, and fibrous anthophyllite asbestos. On the basis of its link with mesothelioma, a more stringent standard of 0.2 fibres/mL was adopted for crocidolite.¹¹ In 1971, the Medical Services Division of HMTI established a prospective mortality study of men in a limited number of workplaces which were covered by the 1969 Asbestos Regulations, subsequently extended to cover most fixed workplaces, and in 1986 to all individuals having statutory medical examinations under the Asbestos Licensing Regulations.¹² 183 mesothelioma deaths occurred in this cohort from 1971 to 91. Over the same period, 10 985 mesothelioma deaths occurred nationally; this figure suggests that the vast majority of workers actually at risk from asbestos were not employed in occupations where this risk was recognised. 24% of male mesothelioma deaths are listed under construction-related occupations in table 3, but the proportion due to exposure in the construction industry is probably considerably higher. Table 3 is based on the most recent full-time occupation as recorded on the death certificate, so men who leave the building industry would not be included in this number. Asbestos imports were at their peak in the 1960s and 1970s (figure 2). In that period the major use of amphibole asbestos was in amosite insulation board used in the construction industry, where monitoring and control of exposure were limited. In addition, more than half the tonnage of chrysotile imported went into products for the construction industry, mainly asbestos cement products and floor tiles.

Most of the asbestos imported to the UK between 1960 and 1980 is still in place in buildings, and carpenters, plumbers, electricians and other workers involved in building renovation, maintenance, and demolition may

still suffer unsuspected exposure. These workers often operate individually or in small unmonitored organisations, and it may be impossible to obtain reliable information on the extent of their exposure. A public information campaign to alert such workers to the potential danger seems justified.

We have confined our analysis to male rates, because there are too few deaths in women at younger ages to provide stable predictions of future mortality. Trends in female rates over the last 25 years have been similar to those in men, although at a much lower level, as would be expected for an occupational cancer (table 1). Death-rates in UK women in 1968-71 were similar to incidence rates in Los Angeles in the 1970s in both men and women with no-suspected asbestos exposure.¹³ This may reflect a spontaneous background risk unrelated to asbestos, although some cases in both sexes may be due to environmental asbestos exposure unrelated to occupation.

The eventual magnitude of the British mesothelioma epidemic is likely to be greater than in the USA. There is no national mesothelioma death registry in the USA, but the SEER cancer incidence data indicate that the USA epidemic has already reached its peak.⁴ Overall incidence increased rapidly during the 1970's, and in the early 1980s male incidence rates were similar to UK death rates in men aged over 65. Since 1980, USA rates have declined in both sexes below age 55, however, and are no longer increasing in men aged under 75, in contrast to the pattern in the UK. Overall numbers in the USA are therefore likely to fall over the next 20 years. The timing of the peak in the USA epidemic reflects the pattern of asbestos use, which reached a plateau soon after World War II.¹⁴

Any contribution of asbestos removal to the mesothelioma epidemic cannot yet be assessed. Asbestos removal did not develop as a specialised industry until the 1980s, and the latency is still too short for these workers to have developed mesothelioma. The campaign to remove all asbestos from schools and other public buildings on the grounds that occupants might be at high risk was founded on fear rather than evidence. Average airborne asbestos levels in such buildings are invariably very low during normal use, and are often unaffected by removal and may even be increased.¹⁴ Whatever its effect on building occupants however, the creation of the new, and initially inadequately regulated, industry of asbestos removal may well have increased the burden of future occupational asbestos disease.

The risk to recent birth cohorts could also be modified by changes in the prevalence of infection with the simian virus SV40, which was a contaminant of poliovaccines which were widely used in the 1950s. According to a recent report,¹⁵ SV40-like DNA sequences are present in most pleural mesotheliomas. Most mesotheliomas containing SV40-like DNA were also associated with asbestos exposure, so this effect, if confirmed, is likely to be synergistic with that of asbestos.

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