Mortality among British asbestos workers undergoing regular medical examinations (1971–2005)

A-H Harding,[1] A Darnton,[2] J Wegerdt,[1] D McElvenny[3,4]

[1] Health and Safety Laboratory, Buxton, Derbyshire, UK; [2] Health and Safety Executive, Bootle, Merseyside, UK; [3] Department of Epidemiology and Genetics, Westlakes Research Institute, Moor Row, Cumbria, UK; [4] Faculty of Health and Social Care, University of Central Lancashire, Preston, Lancashire, UK

Correspondence to:
A-H Harding, Health and Safety Laboratory, Harpur Hill, Buxton, Derbyshire SK17 6RN, UK;
anne-helen.harding@hsl.gov.uk

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ABSTRACT

Objectives: The Great Britain Asbestos Survey was established to monitor mortality among workers covered by regulations to control occupational exposure to asbestos. This study updates the estimated burden of asbestos-related mortality in the cohort, and identifies risk factors associated with mortality.

Methods: From 1971, workers were recruited during initially voluntary and later statutory medical examinations. A brief questionnaire was completed during the medical, and participants were flagged for death registrations. Standardised mortality ratios (SMRs) and proportional mortality ratios (PMRs) were calculated for deaths occurring before 2006. Poisson regression analyses were undertaken for diseases with significant excess mortality.

Results: There were 15 496 deaths among 98 117 workers followed-up for 1 779 580 person-years. The SMR for all cause mortality was 141 (95% CI 139 to 143) and for all malignant neoplasms 163 (95% CI 159 to 167). The SMRs for cancers of the stomach (166), lung (187), peritoneum (3730) and pleura (968), mesothelioma (513), cerebrovascular disease (164) and asbestosis (5594) were statistically significantly elevated, as were the corresponding PMRs. In age and sex adjusted analysis, birth cohort, age at first exposure, year of first exposure, duration of exposure, latency and job type were associated with the relative risk of lung, pleural and peritoneal cancers, asbestosis and mesothelioma mortality.

Conclusions: Known associations between asbestos exposure and mortality from lung, peritoneal and pleural cancers, mesothelioma and asbestosis were confirmed, and evidence of associations with stroke and stomach cancer mortality was observed. Limited evidence suggested that asbestos-related disease risk may be lower among those first exposed in more recent times.

Asbestos has become the leading cause of occupational mortality in Great Britain.[1] Asbestos products first appeared in England in the 1850s and the British asbestos industry began to develop during the 1870s. Medical papers reporting disease among asbestos workers emerged during the 1920s and the first legislation controlling occupational exposure to asbestos in Britain was passed in 1931.[2] This was followed by further regulations aimed at reducing the risk of asbestos-related disease among asbestos workers. Since systematic recording of mesothelioma deaths began in Britain in the late 1960s, the number of annual deaths has increased more than 10-fold, and currently is more than 2000. Despite progressively more stringent laws to reduce occupational exposure, due to long latency, the asbestos-related cancer epidemic in Britain has not yet peaked and substantial numbers of deaths are likely to be seen for a number of decades to come.[3] An estimated 2–3% of lung cancer deaths in Britain in the period 1980–2000 (excluding 1981) may be attributable to asbestos,[4] while the most recent projections suggest that mesothelioma, formerly a very rare cancer, now accounts for around 0.7% of all deaths among men born in the late 1930s or early 1940s.[3]

The Health and Safety Executive's national survey of asbestos workers was established in 1970 in order to monitor the long-term health of workers primarily employed in asbestos product manufacture.[5] Substantial numbers of asbestos removal workers were subsequently recruited and since the decline and eventual ban of asbestos manufacture and use in Britain, these formed the majority of new entrants into the cohort. Mortality up to 1991 has been reported previously.[5] The aim of this study was to update the mortality analysis, including all deaths to the end of 2005, in order to identify risk factors associated with mortality.

METHODS

Survey population

Following approval for the study by the British Medical Association Research Ethics Committee, starting in 1971, workers at factories and workplaces in Great Britain that were covered by the 1969 Asbestos Regulations were invited to participate in the survey. Participants attended a voluntary medical examination at 2-yearly intervals and at the same time completed the survey questionnaire. The 1983 Asbestos Licensing Regulations (ALR) required people who worked with asbestos insulation or asbestos coating to be licensed and to attend statutory medical examinations. These were undertaken before employment and at 2-yearly intervals while the individual was still engaged in this type of work. The 1987 Control of Asbestos at Work Regulations (CAWR) extended the requirement for statutory medicals to all those occupationally exposed to asbestos above a certain action level.[5] Everyone who was medically examined under the 1983 or 1987 regulations became part of the asbestos survey unless they chose to opt out. Consequently, the survey included most licensed asbestos workers in Great Britain.

The survey questionnaire

The questionnaire changed during the course of the survey.[5] Personal details for identification, the date of first exposure to asbestos and smoking history were collected throughout. For workers recruited under the 1983 ALR, no information on job type was collected since they all worked with asbestos insulation or asbestos coating. For the remaining workers, information on the current job was collected. Limited, job-specific information on current asbestos exposure and control practices was recorded for workers recruited under the 1987 CAWR, although this did not include quantitative exposure estimates.

Follow-up

All survey participants were flagged for cancer and death registrations on the National Health Service Central Register (NHSCR) after their first medical. Smoking status and job details were updated when workers attended further medicals.

Job categories

Jobs were classified into four major industrial categories: manufacturing, stripping/removal, ''other exposed'' occupations, and insulation workers. Within these industries there were sectors covering: asbestos textile manufacture; asbestos cement mixture, board and pipe manufacture; asbestos/rubber/resin bitumen mixtures manufacture; asbestos board and paper manufacture; asbestos garment manufacture; dry mixes for insulation and plastering manufacture; maintenance workers in all industries; stripping/removal workers; shipbuilding, repair and breaking; building and construction; and miscellaneous factory processes. The ''other exposed'' workers encompassed the shipbuilding, construction and miscellaneous sectors. For the purposes of the analysis, workers who attended more than one medical were allocated to the job type they had spent most time in. If there was a tie, then the worker was allocated to the job type which was previously reported to have higher mortality.[5]

Causes of death

The causes of death for analysis were selected on the basis of evidence in the literature of an association, or a possible association, with asbestos exposure. The period covered by the survey included deaths coded according to the International Classification of Diseases (ICD) revisions 8 to 10. There was no specific mortality code for mesothelioma before ICD-10, which was introduced for recording of underlying cause of death in Scotland from 2000 and in England and Wales from 2001. Mesothelioma deaths cannot be identified consistently from coded cause of death using earlier ICD revisions since they gave more prominence to tumour site and because ''mesothelioma'' was often recorded on the death certificate without mention of the tumour site. Consequently, mesothelioma was coded to a range of causes, such as lung cancer and cancer of ill-defined and unspecified sites, which typically also included many non-mesothelioma deaths. We therefore restricted the analysis of mesothelioma deaths to those occurring during the period 2001–2005 only. To be consistent with ICD coding in England and Wales, deaths occurring in Scotland during 2000 were recoded to ICD-9.

Statistical analysis

Men and women included in the analysis had valid data on age, sex and date of medical examination, and were between the minimum school leaving age and 85 years of age at their first medical examination. Person-years at risk were calculated from the date of the first medical examination. Standardised mortality ratios (SMRs) were calculated as the ratio of observed to expected deaths, with expected numbers calculated using the 5-year age-, period- and sex-specific mortality rates for Great Britain. To explore issues of potential confounding in the context of the population comparison, in particular by smoking status, proportional mortality ratios (PMRs) were also calculated based on the proportional mortality of each cause of death in Great Britain. SMRs and PMRs were calculated using OCMAP-PLUS V4·00 (Release 01e) (Department of Biostatistics, University of Pittsburgh, Pittsburgh, PA). To further explore the issue of confounding, and to investigate the risk factors associated with mortality, internal analysis was undertaken using Poisson regression with Stata SE v 10.1 software (StataCorp LP, College Station, TX). Those causes of death which indicated a statistically significant excess mortality in the SMR and PMR analysis or statistically significantly raised SMR and non-significant PMR, were included in the internal analysis. The potential explanatory variables tested were age, sex, calendar period of death, birth cohort, year of first exposure, age at first exposure, length of exposure, latency (years since first occupational exposure), smoking status, main job, and whether a short- or longer-term worker. Workers were classed as longer-term if they had attended more than one medical and short-term otherwise. The first level of any categorical variable was used as the reference category, unless there were less than five deaths in this category. When this occurred, the second level of the variable was used as the reference category. Changing the reference category did not alter the nature of the association with mortality, but it did increase the precision of the estimates. The model including age and sex was the starting point for the internal analysis. Separate models for each explanatory variable, adjusted for age and sex, were then fitted. The combined effects of variables were examined by including more than one explanatory variable at a time in the model adjusted for age and sex (full results not shown). The final models selected included variables which made a statistically significant contribution to the model ($p \leqslant 0.05$) and which had stable coefficients. Near collinearity between time-related variables, such as age, age at first exposure and latency, led to unstable regression coefficients when they were included in the model simultaneously. Since asbestos-related diseases typically have a long latency, short-term follow-up beyond first exposure will be largely uninformative, and its inclusion may dilute any observed associations. In order to check for this, the age and sex adjusted analysis of each explanatory variable was repeated by restricting the analysis to those individuals with at least 20 years' follow-up. In the restricted analysis, person-years' follow-up started accumulating after 20 years' follow-up had been reached. Significance of model parameters was determined using the likelihood ratio test, and model goodness of fit was tested.

RESULTS

Altogether, 99 588 men and women completed 209 329 survey questionnaires from the start of the survey in 1971 to the end of 2005. Of these, 98% were successfully traced for follow-up through the NHSCR. With exclusions for incomplete data, age less than the minimum school leaving age (n = 13) or age greater than 85 years (n = 1) at the first medical examination, 98 117 individuals remained in the analysis.

Overall, 95% of the cohort was male, and at the time of the medical examinations 5% of the workers were based in Scotland. The mean age at the first medical examination was 35 years (SD 12) (table 1). At the last recorded medical, 53% of men and 47% of women were current smokers. Overall, 57% of survey participants attended one medical examination only, while the remaining workers attended between two and 19 medicals. In 1975, 62% of participants were employed in the asbestos manufacturing industry and 5% in the asbestos removal industry (fig 1). By 2005, the manufacturing industry had ceased and 94% of workers were employed in the asbestos removal industry. The majority of manufacturing workers joined the survey before 1984, while the majority of removal workers joined after 1984.

Standardised and proportional mortality ratio analyses

There was a statistically significant excess of deaths from all causes among the asbestos workers (SMR 141; 95% CI 139 to 143) (table 2). SMRs were also statistically significantly elevated for all malignant neoplasms, cancers of the oesophagus, stomach, colon, rectum, liver, larynx, lung, peritoneum, pleura, kidney and bladder, mesothelioma, circulatory diseases and respiratory disease including asbestosis. PMRs for all malignant neoplasms, cancers of the stomach, lung, peritoneum and pleura, and mesothelioma, cerebrovascular disease and asbestosis were significantly elevated above 100; PMRs for cancers of the colon, rectum, liver, larynx, bladder and kidney were not statistically significant.

Asbestosis mortality

Poisson regression analysis indicated that, adjusted for age and sex, the following were statistically significantly associated with asbestosis mortality: birth cohort, year first occupationally exposed to asbestos, age first exposed, length of exposure, latency, smoking status at the last medical examination and main job (table 3). When entered into the model simultaneously, only year first exposed, smoking status and main job were statistically significant in the final model. The relative risk of asbestosis was significantly lower for workers first exposed after 1959 than for workers first exposed before 1960 (RR 0.11 for first exposure in 1960–69 compared to 1930–39 in the final model, 95% CI 0.03 to 0.38). Current and former smokers had similar relative risks of asbestosis, which were more than three times higher than the relative risk for never smokers. Insulation workers had the highest risk of asbestosis: RR 5.98 (95% CI 3.84 to 9.31) compared to manufacturing workers, followed by removal workers (RR 2.21; 95% CI 1.24 to 3.93).

Cerebrovascular disease mortality

In the analysis adjusted for age and sex, the following were statistically significantly associated with stroke mortality: birth cohort, year first occupationally exposed to asbestos, smoking status and main job (table 3). Main job was no longer statistically significant in the final model in which variables were included simultaneously. The relative risk of stroke decreased in later birth cohorts and for workers first exposed in more recent years. Current smokers, but not former smokers, had a significantly increased risk of mortality compared with never smokers (RR 1.56 in the final model; 95% CI 1.29 to 1.89).

Lung cancer mortality

In models adjusted only for age and sex, the following were statistically significantly associated with lung cancer mortality: period of death, birth cohort, year first occupationally exposed to asbestos, age at first exposure, length of exposure, latency, smoking status and main job (table 3). In the final model with variables included simultaneously, cohort, year first exposed, latency, smoking status and main job were statistically significant. The relative risk of lung cancer decreased steadily from the oldest to the youngest cohort, and for those first exposed in later years, with relative risks very similar to those observed in the analysis adjusted for age and sex. Current and former smokers had a higher risk of lung cancer (RR 14.3 in the final model; 95% CI 10.2 to 20.1, and RR 4.55; 95% CI 3.20 to 6.46, respectively) than never smokers. Insulation workers and removal workers had significantly higher risks of lung cancer than manufacturing workers (RR 1.84 in the final model; 95% CI 1.60 to 2.10, and RR 1.30; 95% CI 1.12 to 1.50, respectively).

Stomach cancer mortality

Adjusted for age and sex, the following were statistically significantly associated with stomach cancer mortality: period

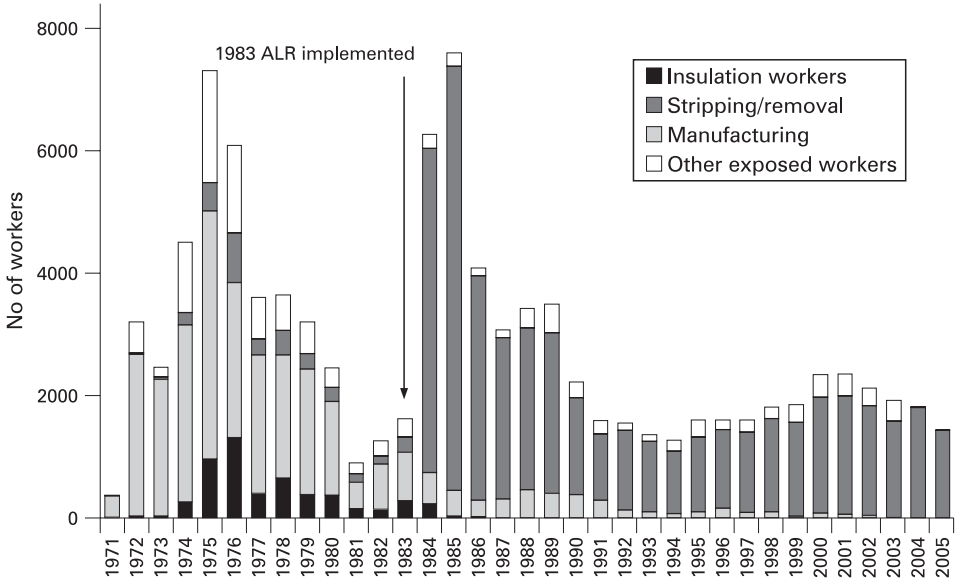

Figure 1 Number of workers recruited into the survey each year, by main job (1971–2005). ALR, Asbestos Licensing Regulations.

Table 1 The Great Britain Asbestos Survey population (1971–2005)

	Men	Women
Number of individuals	93622	4495
Person-years at risk	1676186	103394
Age (at first exam, years)	35 (SD 12)	36 (SD 13)
Current smokers (at last exam)	50036 (53%)	2115 (47%)
Attended one exam only (short-term worker)	53294 (57%)	2400 (53%)
Main industry categories*		
Manufacturing workers	25674 (28%)	2895 (65%)
Removal workers	49885 (54%)	599 (13%)
"Other" exposed workers	11996 (13%)	819 (18%)
Insulation workers	5039 (5%)	173 (4%)

*Information on job type was available for 97 080 workers.

of death, birth cohort, year first occupationally exposed to asbestos, smoking status and main job (table 4). In the final model, birth cohort and smoking status were statistically significant. The relative risk of stomach cancer fell in the younger birth cohorts (RR for the 1950–59 cohort compared to the <1920 cohort in the final model: 0.11; 95% CI 0.05 to 0.24), and there were no deaths from stomach cancer among workers born after 1960. Current smokers, but not former smokers, had an increased risk of mortality (RR 1.42; 95% CI 1.00 to 2.02) compared to never smokers.

Pleural and peritoneal cancer mortality

Although the relative risks were larger in the peritoneal cancer analysis, the variables associated with mortality were similar for pleural and peritoneal cancers. In the analysis adjusted for age and sex only, period, birth cohort, year first exposed, age at first exposure, length of exposure, latency and main job were statistically significantly associated with the relative risk of pleural cancer and peritoneal cancer mortality, and smoking status was statistically significantly associated with peritoneal cancer mortality (table 4). In the final model with variables included simultaneously, period of death, length of exposure and main job were statistically significant. In these models, compared to workers with less than 10 years' exposure, the relative risk of pleural cancer was 4.35 (95% CI 2.18 to 8.68) and of peritoneal cancer 14.9 (95% CI 5.80 to 38.5) for workers with at least 40 years' occupational exposure to asbestos. Manufacturing workers had lower risks of both cancers than other workers. Compared with manufacturing workers, for insulation and removal workers the relative risks of pleural cancer were 3.19 (95% CI 2.04 to 5.01) and 1.61 (95% CI 0.98 to 2.64), respectively, and the relative risks of peritoneal cancer were 20.6 (95% CI 9.53 to 44.6) and 9.69 (95% CI 4.28 to 21.9), respectively.

Mesothelioma mortality

Period of death could not be analysed for mesothelioma mortality since deaths were only identified in one period. This also resulted in birth cohort and age being highly correlated and so they were not included together in any of the models. In age and sex adjusted models, the following were statistically significantly associated with mesothelioma mortality: year first exposed, age first exposed, length of exposure, latency, main job and short/longer-term worker. In the final model when explanatory variables were included in the model simultaneously, only latency and main job were statistically significant. The relative risk of mesothelioma increased with latency, reaching a maximum 50–59 years after first exposure (RR for 50–59 years' latency compared with <20 years': 28.1; 95% CI 12.2 to 64.6). Removal workers and insulation workers had the highest relative risk of mesothelioma (RR 3.19; 95% CI 2.16 to 4.72 compared with manufacturing workers in the final model, and RR 2.65; 95% CI 1.64 to 4.30, respectively).

Table 2 Mortality among the Great Britain Asbestos Survey workers (1971–2001)

Cause of death	Observed no of deaths	Standardised mortality ratio (95% CI)	Proportional mortality ratio (95% CI)
All causes	15496	141 (139 to 143)	–
All malignant neoplasms	5529	163 (159 to 167)	113 (111 to 116)
MN of lip, oral cavity and pharynx	74	106 (83 to 133)	73 (58 to 92)
MN of oesophagus	220	116 (101 to 132)	83 (73 to 95)
MN of stomach	322	166 (149 to 186)	114 (102 to 127)
MN of colon	297	128 (114 to 144)	90 (80 to 100)
MN of rectum	183	151 (130 to 174)	100 (86 to 115)
MN of liver (primary)	83	137 (109 to 170)	101 (81 to 125)
MN of larynx	49	148 (109 to 195)	101 (76 to 134)
MN of lung	1882	187 (179 to 196)	129 (123 to 134)
MN of peritoneum	85	3730 (2979 to 4612)	2246 (1941 to 2599)
MN of pleura	137	968 (817 to 1139)	568 (492 to 656)
Mesothelioma*	160	513 (435 to 601)	489 (424 to 564)
MN of breast	52	112 (66 to 180)	58 (45 to 75)
MN of ovary	17	112 (66 to 180)	68 (43 to 108)
MN of kidney	114	153 (126 to 183)	101 (84 to 122)
MN of bladder	155	145 (123 to 170)	103 (84 to 122)
MN of lymphatic and haematopoietic tissue	298	102 (90 to 114)	74 (66 to 82)
Circulatory disease	6170	141 (138 to 145)	97 (96 to 99)
Ischaemic heart disease	4183	140 (136 to 144)	95 (93 to 97)
Cerebrovascular disease	1049	164 (154 to 174)	115 (109 to 122)
Respiratory disease	1561	162 (154 to 170)	118 (113 to 124)
Asbestosis	119	5594 (4634 to 6694)	3944 (3541 to 4393)

*ICD-10 mesothelioma (deaths 2001–2005).
MN, malignant neoplasm.

Poisson regression analysis of causes of death with significantly raised SMR but non-significant PMR

In Poisson regression analysis adjusted for age and sex, the associations observed with potential explanatory variables were generally weak, and the associations tended not to be with variables specifically related to asbestos exposure, namely length of exposure and main job. Colon cancer mortality was associated with birth cohort, year exposed, age exposed, smoking status and main job; bladder cancer mortality was associated with period, cohort, year exposed and smoking status; laryngeal cancer was associated with age exposed, length of exposure and smoking status; cancer of the rectum was associated with cohort and main job; and kidney cancer mortality was associated with latency. There were no statistically significant associations with liver cancer mortality.

Analysis restricted to death with a minimum of 20 years' latency

The separate age and sex adjusted analysis of each explanatory variable was repeated with deaths restricted to those occurring at least 20 years after first occupational exposure to asbestos (results not shown). The trends observed in the restricted analysis tended to be stronger than those in the unrestricted

Table 3 Relative risk of asbestosis, cerebrovascular disease and lung cancer mortality, adjusted for age and sex

	Asbestosis		Cerebrovascular disease		Lung cancer	
Risk factor	Deaths	Relative risk (95% CI)	Deaths	Relative risk (95% CI)	Deaths	Relative risk (95% CI)
Period						
<1980	7	1.00	42	1.00	123	1.00
1980–89	32	0.87 (0.38 to 1.99)	218	0.90 (0.71 to 1.38)	509	0.89 (0.73 to 1.08)
1990–99	42	0.52 (0.23 to 1.18)	460	0.95 (0.69 to 1.31)	692	0.59 (0.49 to 0.72)
>2000	38	0.52 (0.23 to 1.19)	329	0.75 (0.54 to 1.04)	558	0.54 (0.44 to 0.66)
Cohort						
<1920	33	1.00	381	1.00	473	1.00
1920–29	50	0.82 (0.53 to 1.28)	381	0.56 (0.48 to 0.65)	677	0.74 (0.66 to 0.84)
1930–39	28	0.59 (0.34 to 1.03)	183	0.39 (0.32 to 0.47)	447	0.57 (0.49 to 0.65)
1940–49	7	0.23 (0.09 to 0.59)	64	0.25 (0.18 to 0.34)	227	0.39 (0.32 to 0.47)
1950–59	1	0.06 (0.01 to 0.50)	30	0.25 (0.16 to 0.39)	53	0.14 (0.10 to 0.20)
1960–69	0	–	9	0.24 (0.12 to 0.51)	5	0.03 (0.01 to 0.08)
1970–79	0	–	1	0.28 (0.04 to 2.04)	0	–
Year first exposed						
<1930	3	2.65 (0.76 to 9.31)	15	1.00	12	1.00
1930–39	13	1.00	78	0.48 (0.28 to 0.83)	114	0.83 (0.46 to 1.50)
1940–49	26	0.89 (0.46 to 1.74)	127	0.36 (0.21 to 0.62)	247	0.80 (0.45 to 1.43)
1950–59	46	0.94 (0.50 to 1.74)	156	0.29 (0.17 to 0.49)	379	0.73 (0.41 to 1.30)
1960–69	18	0.24 (0.12 to 0.50)	275	0.35 (0.21 to 0.59)	429	0.55 (0.31 to 0.98)
1970–79	11	0.11 (0.05 to 0.26)	317	0.33 (0.20 to 0.56)	526	0.52 (0.29 to 0.92)
1980–89	2	0.05 (0.01 to 0.24)	72	0.23 (0.13 to 0.42)	156	0.38 (0.21 to 0.70)
>1990	0	–	9	0.13 (0.06 to 0.30)	19	0.17 (0.08 to 0.36)
Age first exposed (years)						
<20	39	1.00	124	1.00	328	1.00
20–29	33	0.53 (0.33 to 0.84)	189	0.96 (0.76 to 1.20)	356	0.66 (0.57 to 0.77)
30–39	23	0.33 (0.20 to 0.55)	240	1.10 (0.89 to 1.37)	450	0.82 (0.71 to 0.95)
40–49	17	0.22 (0.12 to 0.39)	289	1.21 (0.98 to 1.50)	451	0.82 (0.71 to 0.95)
>50	7	0.12 (0.05 to 0.26)	207	1.19 (0.95 to 1.50)	297	0.78 (0.66 to 0.92)
Length of exposure (years)						
<10	2	1.00	88	1.00	193	1.00
10–19	15	4.20 (0.95 to 18.6)	234	1.12 (0.87 to 1.43)	413	1.13 (0.95 to 1.34)
20–29	21	5.17 (1.18 to 22.6)	268	0.95 (0.74 to 1.22)	471	1.09 (0.91 to 1.30)
30–39	26	8.99 (2.06 to 39.2)	196	0.92 (0.71 to 1.20)	397	1.27 (1.06 to 1.53)
>40	55	19.7 (4.51 to 85.6)	263	1.10 (0.84 to 1.42)	408	1.30 (1.07 to 1.57)
Latency (years since first exposure)						
<20	13	1.00	248	1.00	512	1.00
20–29	17	1.57 (0.75 to 3.30)	280	1.01 (0.85 to 1.20)	457	0.98 (0.86 to 1.11)
30–39	26	3.12 (1.54 to 6.31)	220	0.95 (0.78 to 1.14)	413	1.11 (0.97 to 1.28)
40–49	29	5.34 (2.59 to 11.0)	155	0.94 (0.76 to 1.16)	310	1.24 (1.06 to 1.44)
50–59	27	10.4 (4.80 to 22.3)	99	1.07 (0.83 to 1.37)	156	1.24 (1.02 to 1.50)
>60	7	12.0 (4.34 to 33.0)	47	2.10 (1.51 to 2.90)	34	1.18 (0.82 to 1.68)
Smoking status						
Never	7	1.00	136	1.00	36	1.00
Former	47	3.58 (1.61 to 7.96)	254	1.03 (0.84 to 1.27)	311	4.93 (3.49 to 6.98)
Current	64	3.25 (1.49 to 7.10)	630	1.70 (1.41 to 2.04)	1474	14.9 (10.7 to 20.7)
Main job						
Manufacturing	39	1.00	641	1.00	930	1.00
Removal	21	1.46 (0.84 to 2.51)	135	0.59 (0.50 to 0.72)	355	0.87 (0.76 to 0.98)
"Other"	17	1.23 (0.70 to 2.18)	184	0.82 (0.70 to 0.97)	296	0.89 (0.78 to 1.02)
Insulation	42	6.88 (4.45 to 10.7)	86	0.88 (0.70 to 1.10)	286	1.91 (1.68 to 2.18)
Short/longer-term worker (reference category short-term)						
Short-term	58	1.00	505	1.00	892	1.00
Long-term	61	0.88 (0.61 to 1.26)	544	0.90 (0.79 to 1.01)	990	0.94 (0.86 to 1.03)

analysis. However, with some exceptions, the restricted analysis did not change the conclusions about which explanatory variables were important. Changes in the observed associations occurred in the association between age at first exposure and the risk of stroke and the risk of stomach cancer; in the restricted analysis adjusted for age and sex, the relative risks of mortality were significantly lower for workers first exposed at older ages. In addition, statistically significant positive associations were observed between duration of exposure and stroke mortality, and between latency and the risk of stomach cancer.

Table 4 Relative risk of stomach, pleural and peritoneal cancer and mesothelioma mortality, adjusted for age and sex

	Stomach cancer		Pleural cancer		Peritoneal cancer		Mesothelioma*	
Risk factor	Deaths	Relative risk (95% CI)	Deaths	Relative risk (95% CI)	Deaths	Relative risk (95% CI)	Deaths	Relative risk (95% CI)
Period								
<1980	26	1.00	9	1.00	7	1.00	0	–
1980–89	96	0.79 (0.51 to 1.22)	55	1.42 (0.70 to 2.89)	36	1.26 (0.56 to 2.83)	0	–
1990–99	132	0.53 (0.34 to 0.81)	64	0.86 (0.42 to 1.73)	40	0.75 (0.33 to 1.68)	0	–
>2000	68	0.31 (0.19 to 0.48)	9	0.14 (0.06 to 0.36)	2	0.04 (0.01 to 0.22)	160	–
Cohort								
<1920	90	1.00	28	1.00	11	1.00	6	1.00†
1920–29	115	0.65 (0.49 to 0.85)	54	0.84 (0.53 to 1.34)	31	1.13 (0.56 to 2.27)	30	1.98 (0.82 to 4.76)
1930–39	77	0.46 (0.33 to 0.65)	35	0.44 (0.26 to 0.77)	30	0.76 (0.36 to 1.61)	58	2.64 (1.14 to 6.12)
1940–49	29	0.21 (0.13 to 0.35)	17	0.18 (0.09 to 0.38)	12	0.21 (0.08 to 0.57)	54	1.73 (0.74 to 4.02)
1950–59	11	0.12 (0.06 to 0.25)	3	0.03 (0.01 to 0.12)	1	0.02 (0.002 to 0.13)	10	0.27 (0.10 to 0.74)
1960–69	0	–	0	–	0	–	2	0.08 (0.02 to 0.41)
Year first exposed								
<1930	2	1.01 (0.24 to 4.25)	1	0.73 (0.10 to 5.50)	0	–	0	–
1930–39	23	1.00	17	1.00	9	1.00	0	–
1940–49	31	0.60 (0.35 to 1.03)	24	0.57 (0.31 to 1.07)	25	1.01 (0.47 to 2.16)	11	1.00
1950–59	59	0.68 (0.42 to 1.10)	40	0.49 (0.27 to 0.86)	32	0.54 (0.25 to 1.16)	60	3.22 (1.69 to 6.13)
1960–69	79	0.61 (0.38 to 0.97)	27	0.19 (0.10 to 0.35)	8	0.06 (0.02 to 0.17)	47	1.71 (0.88 to 3.31)
1970–79	103	0.61 (0.38 to 0.97)	21	0.09 (0.05 to 0.18)	8	0.03 (0.01 to 0.09)	27	0.76 (0.37 to 1.54)
1980–89	24	0.35 (0.19 to 0.64)	7	0.05 (0.02 to 0.14)	3	0.02 (0.003 to 0.07)	11	0.76 (0.32 to 1.80)
>1990	1	0.05 (0.01 to 0.40)	0	–	0	–	4	1.02 (0.31 to 3.31)
Age first exposed (years)								
<20	41	1.00	45	1.00	49	1.00	69	1.00
20–29	68	1.01 (0.69 to 1.49)	44	0.59 (0.39 to 0.90)	21	0.26 (0.15 to 0.43)	41	0.36 (0.25 to 0.54)
30–39	80	1.18 (0.81 to 1.72)	18	0.25 (0.14 to 0.43)	5	0.06 (0.03 to 0.16)	26	0.22 (0.14 to 0.34)
40–49	79	1.17 (0.80 to 1.72)	12	0.17 (0.09 to 0.33)	3	0.04 (0.01 to 0.14)	13	0.10 (0.06 to 0.19)
>50	54	1.15 (0.76 to 1.75)	18	0.39 (0.22 to 0.68)	7	0.15 (0.07 to 0.34)	11	0.12 (0.06 to 0.23)
Length of exposure (years)								
<10	33	1.00	17	1.00	10	1.00	4	1.00
10–19	85	1.33 (0.88 to 2.01)	8	0.36 (0.15 to 0.83)	1	0.12 (0.01 to 0.93)	8	1.60 (0.48 to 5.38)
20–29	81	1.06 (0.70 to 1.63)	37	1.75 (0.94 to 3.08)	15	2.68 (1.10 to 6.55)	28	6.27 (2.12 to 18.5)
30–39	58	1.05 (0.66 to 1.64)	38	2.86 (1.49 to 5.49)	27	9.87 (3.97 to 24.6)	42	15.2 (5.16 to 45.0)
>40	65	1.15 (0.72 to 1.83)	37	3.54 (1.74 to 7.23)	32	21.6 (7.69 to 60.6)	78	37.6 (12.4 to 114)
Latency (years since first exposure)								
<20	98	1.00	24	1.00	10	1.00	10	1.00
20–29	87	0.95 (0.70 to 1.28)	31	2.08 (1.19 to 3.64)	12	3.47 (1.43 to 8.44)	20	3.36 (1.54 to 7.33)
30–39	65	0.88 (0.63 to 1.22)	35	3.45 (1.95 to 6.11)	25	14.1 (5.99 to 33.4)	45	11.2 (5.40 to 23.4)
40–49	42	0.83 (0.57 to 1.22)	36	6.22 (3.40 to 11.4)	28	37.0 (14.4 to 94.9)	54	23.9 (11.2 to 51.1)
50–59	23	0.89 (0.55 to 1.45)	11	4.61 (2.04 to 10.4)	9	39.2 (12.1 to 127)	29	31.9 (13.7 to 74.0)
>60	7	1.18 (0.54 to 2.60)	0	–	1	24.7 (2.68 to 228)	2	10.7 (2.17 to 52.6)
Smoking status‡								
Never	39	1.00	18	1.00	10	1.00	29	1.00
Former	102	1.50 (1.03 to 2.17)	41	1.47 (0.84 to 2.58)	33	2.27 (1.11 to 4.65)	51	0.97 (0.61 to 1.55)
Current	170	1.58 (1.12 to 2.24)	69	1.45 (0.86 to 2.44)	39	1.50 (0.75 to 3.00)	77	0.94 (0.61 to 1.44)
Main job‡								
Manufacturing	174	1.00	52	1.00	8	1.00	48	1.00
Removal	44	0.63 (0.44 to 0.92)	29	1.06 (0.66 to 1.69)	30	6.38 (2.88 to 14.1)	65	3.30 (2.23 to 4.86)
"Other"	71	1.08 (0.77 to 1.50)	24	1.28 (0.79 to 2.08)	9	3.06 (1.18 to 7.92)	19	1.11 (0.65 to 1.88)
Insulation	32	1.30 (0.84 to 2.01)	31	3.60 (2.30 to 5.62)	36	26.1 (12.1 to 56.1)	26	3.37 (2.09 to 5.44)
Short/longer-term worker (reference category short-term)								
Short-term	147	1.00	56	1.00	34	1.00	59	1.00
Long-term	175	1.01 (0.81 to 1.26)	81	1.27 (0.90 to 1.78)	51	1.35 (0.88 to 2.09)	101	1.46 (1.06 to 2.01)

*ICD-10 mesothelioma deaths (2001–2005); †cohort only adjusted for sex due to collinearity with age; ‡missing values occurred in this variable.

DISCUSSION

The Great Britain Asbestos Survey is one of the largest and longest running surveys undertaken on asbestos workers in the world. It includes a substantial proportion of workers in asbestos product manufacture since 1970 and most asbestos workers undergoing statutory medical surveillance. This analysis demonstrated convincing evidence of increased mortality from cancers of the lung, peritoneum and pleura, mesothelioma and asbestosis, and provided some evidence of an association between asbestos exposure and mortality from stroke and stomach cancer. Less convincing evidence of an association with asbestos was observed for cancers of the colon and the larynx, but for other causes of death there was insufficient evidence to support an association with occupational exposure to asbestos.

The SMRs were likely to be confounded by other risk factors, particularly smoking. Over 50% of the Great Britain asbestos workers were current smokers. When broken down by year of medical examination, the proportion of current smokers remained at over 50% throughout the survey period. Smoking prevalence among the asbestos workers was similar to the Great Britain population in the early 1970s, but by 2005, the prevalence of smoking in the Great Britain population had fallen to 24%.[6] Smoking is associated with many cancers, as well as respiratory and circulatory diseases.[7] Several causes of death associated with smoking had statistically significantly raised SMRs but did not have statistically significantly raised PMRs, which suggests that the observed excesses might be due to confounding factors such as smoking rather than to asbestos exposure. This was the case for cancers of the oesophagus, colon, rectum, liver, larynx, kidney and bladder, and for circulatory disease overall. However, some caution is required since the PMR analysis cannot be considered to be a formal adjustment for confounding factors. Poisson regression analysis confirmed that smoking status was associated with mortality from cancers of the colon, larynx and bladder.

The SMR/PMR analysis added to the body of evidence, which consistently shows that asbestos exposure is associated with excess mortality from lung, pleural and peritoneal cancers, asbestosis and mesothelioma.[4 8–12] The internal analysis showed that year of first occupational exposure to asbestos, age at first exposure, duration of exposure, latency and job type were all associated with mortality in the age and sex adjusted models. Together the SMR/PMR and Poisson regression analyses provided convincing evidence of the association between occupational exposure to asbestos and increased mortality from these diseases.

The Poisson regression analysis gave some indication that the relative risk of these diseases may be falling among workers first exposed in more recent times and in later birth cohorts; the relative risks of asbestosis, lung, pleural and peritoneal cancers were lower for workers born after 1939 and workers first exposed after 1959. This may be a consequence of progressively more stringent laws to reduce occupational exposure to asbestos, starting with the Asbestos Regulations in 1969. However, it may also reflect the long latency of these diseases whereby the highest risks occur 40 or more years after first exposure. The introduction of a separate ICD code for mesothelioma may have resulted in spurious trends with time. The large fall in the relative risks of pleural and peritoneal cancers in the calendar period 2000–2005 was likely to be a consequence of pleural and peritoneal mesotheliomas being coded to the new ICD-10 code for mesothelioma after 2001, leaving only pleural and peritoneal cancers in these two cause of death categories.

An excess of deaths from cerebrovascular disease and from stomach cancer was observed among the Great Britain asbestos workers, and the Poisson regression analysis provided some evidence of an association with asbestos exposure. In the restricted Poisson regression, where observed effects tended to be stronger, birth cohort, year of first exposure, age at first exposure, duration of exposure (stroke only) and latency (stomach cancer only) were statistically significantly associated with mortality.

Elevated risk of stroke has been reported in a number of asbestos-exposed cohorts,[13–15] but a large study of Swedish construction workers found no association between exposure to inorganic dust, including asbestos, and stroke.[16] The published evidence for an association between stomach cancer and asbestos exposure is also inconclusive.[17] The 1987 IARC[18] review of the strength of evidence for a causal relationship between asbestos exposure and gastrointestinal cancer found "sufficient" evidence, while the 2006 US Institute of Medicine (US IoM) Committee on Asbestos[19] found the evidence was "suggestive but not sufficient". On the other hand, there is strong evidence that stroke and stomach cancer are associated with smoking.[20–22] The excess mortality from stroke and stomach cancer observed in this cohort is likely to be at least partially attributable to smoking and other risk factors; however, there was also some evidence of an association with asbestos exposure.

The SMR/PMR analysis included other diseases which have been linked with asbestos or studied in asbestos-exposed cohorts. There is "sufficient" evidence to infer a causal relationship between asbestos exposure and laryngeal cancer according to both IARC[18] and US IoM[19] reviews; however, the results from the Great Britain asbestos workers were not consistent with there being a strong relationship between asbestos exposure and laryngeal cancer or other cancers of the upper respiratory tract. Similarly, the results in relation to colorectal cancer were not consistent with a strong effect due to asbestos. Among the Great Britain asbestos workers, mortality from laryngeal and colorectal cancers was more likely to be due to smoking and other established risk factors,[23] although an association with asbestos exposure could not be ruled out.

The analysis has some important limitations. The mortality analysis was based on the underlying cause of death as reported on death certificates. Consequently, the true burden of some asbestos-related diseases may have been underestimated, although the SMRs were unlikely to be biased. For individuals with asbestosis or mesothelioma, the underlying cause of death is often not recorded as asbestosis or mesothelioma. Since asbestosis is a chronic condition, many deceased individuals with asbestosis are assigned a different underlying cause of death. The Great Britain Asbestosis Register shows that of the 373 deaths with asbestosis mentioned on the death certificate in 2005, 134 deaths had underlying cause recorded as asbestosis.[24] Before the use of ICD-10 many mesotheliomas were not recorded as pleural or peritoneal cancer as the underlying cause of death,[5 25] but were coded as malignant neoplasm of ill-defined, secondary and unspecified sites. Furthermore, the majority of national deaths recorded as pleural cancer as the underlying cause prior to the use of ICD-10 were in fact mesotheliomas, but only a minority (approximately 20% during the period 1979–1999) of national deaths recorded as peritoneal cancer were mesotheliomas. The results for peritoneal cancer therefore cannot be taken to describe peritoneal mesothelioma alone. Misclassification of mesothelioma deaths may have occurred beyond the introduction of ICD-10 with some pleural mesotheliomas being misdiagnosed as lung cancers, and peritoneal mesotheliomas being misdiagnosed as gastrointestinal cancers.[26]

The survey collected no information on potentially important risk factors such as diet and physical activity, and only limited information on exposure to asbestos. Participation in the survey was assumed to imply occupational exposure to asbestos; no direct information was available for all the workers about important determinants of risk such as type of asbestos, intensity and length of exposure,[27 28] although job type gave some insight into exposures. Clear differences in mortality were observed between job types. Insulation, and to a lesser degree removal and "other" exposed workers, in the Great Britain survey were at higher risk of mortality than manufacturing workers. Employment in the asbestos insulation industry was

Main messages

- The analysis confirmed known associations between asbestos exposure and mortality from asbestosis, lung, pleural and peritoneal cancers and mesothelioma, and provided some evidence of an association with stroke and stomach cancer mortality; it did not provide conclusive evidence to support a priori suspected associations between asbestos exposure and other causes of death.
- Insulation workers had the highest mortality from asbestos-related diseases; although asbestos removal is a relatively recent development in the asbestos industry, mortality among removal workers was higher than among manufacturing workers.
- Smoking was an important risk factor for asbestosis and for lung cancer but not for the mesotheliomas.

Policy implications

- A strategy for smoking cessation among asbestos workers would have potentially large health benefits.
- Some evidence is emerging that asbestos legislation is beginning to have an impact on the level of disease.
- Continued surveillance of asbestos workers is essential in order to monitor the effectiveness of regulations to control occupational exposure to asbestos in reducing asbestos-related mortality.

likely to involve exposure to substantial quantities of amphibole asbestos. Except in populations with high amphibole exposures,[27 29] the incidence of pleural mesothelioma is typically an order of magnitude greater than that of peritoneal mesothelioma.[10] The ratios of peritoneal to pleural cancers found in the insulation and removal workers in this study were about 1:1, which was suggestive of high amphibole exposure among these groups. For manufacturing and "other" exposed workers, the ratios were approximately 1:6 and 1:4, respectively.

The length of follow-up was both a strength and a limitation of the survey. Workers recruited at the beginning of the survey had up to 35 years' follow-up. For them, the full extent of the burden of asbestos-related disease is now emerging. The mortality experience of those employed in the asbestos stripping/removal industry is of particular interest given the rapid expansion of this industry during the mid-1980s. For most of these workers, there was less than 20 years' follow-up, which was insufficient to determine the full extent of diseases with a long latent period. Consequently, it was not possible to demonstrate conclusively any effects on mortality of changes in control practice since the introduction of the 1983 ALR or later regulations.

Conclusion

The asbestos-exposed workers included in this study did not demonstrate the usual healthy-worker effect but experienced statistically significantly higher mortality than the Great Britain population, and greatly increased mortality for a number of specific causes of death. Increased mortality from certain causes may be attributable at least in part to smoking, since a large proportion of the cohort were current or former smokers. The analysis confirmed known associations between asbestos exposure and mortality from asbestosis, lung, pleural and peritoneal cancers and mesothelioma, and provided evidence of associations between asbestos exposure and stroke and stomach cancer mortality, but there was no conclusive evidence of other a priori suspected associations with asbestos exposure, such as laryngeal cancer. Elevated mortality from these diseases was more likely to be attributable to smoking and other risk factors than to asbestos exposure. The study provided some evidence that as a result of legislation to reduce occupational exposure to asbestos, the risk of asbestos-related disease mortality may be lower among those first occupationally exposed to asbestos in more recent times, but due to the long latency of these diseases further follow-up is required to confirm this trend.

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