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Asbestos and cancer: a cohort followed up to death

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ABSTRACT The mortality experience of 1074 white men who retired from a United States asbestos company during the period 1941–67 and who were exposed to asbestos working as production and maintenance employees for the company is reported to the end of 1980 when 88% of this cohort was known to be dead. As noted in earlier reports the mortality for respiratory and gastrointestinal cancer was raised. A more detailed examination of causes of death shows that the excess in gastrointestinal cancer was largely due to a statistically significant excess in stomach cancer. A statistically significant excess was also noted for kidney cancer, cancer of the eye, and non-malignant respiratory disease. Eight deaths from malignant mesothelioma were observed, two of which were peritoneal. Asbestos exposures for these mesothelioma cases were low relative to other members of the cohort. Continuing follow up of this cohort shows a dose response relation for respiratory cancer that has become increasingly linear. Standardised mortality ratios peaked 10 to 15 years after retirement and were relatively constant at around 250 in each five year interval starting in 1950. This excess might have been detected as early as 1960 but certainly by 1965. The mortality experience of this cohort reflects the ultimate effects of asbestos since nearly all of the cohort has now died.

Several reports have been made on the mortality experience of a cohort of asbestos workers who retired from a large asbestos products company in the United States.[1–4] The cohort consisted of men who retired during the years 1941–67 and who completed their working lifetime as production or maintenance employees of the asbestos company. All were exposed to asbestos fibres in varying degrees during their employment. Follow up started at age 65 or at the date retirement began if older than 65; men who retired before 65 but lived to 65 are also included. The average duration of employment was 25 years (range 3–51 years). For each worker an estimate was made of his level of asbestos exposure based on measures of dust expressed in million particles per cubic foot obtained from environmental hygiene surveys that started in the mid-1950s and which were extrapolated back in time by the company industrial hygienist. Consideration was given to process changes, machine installations, ventilation control expenditures, and judgmental determinations.

In the earliest reports the mortality experience was followed up to 1969 as reflected in records maintained by the company and included workers from 13 locations of which two were Canadian: Toronto, Ontario, and Asbestos, Quebec. A later report on the mortality experience to 1973 dealt with only those workers employed within the United States. For that report follow up for death was based on the records maintained by the United States Social Security System. The present study reports on the mortality experience to 1980 and is based on records maintained by the social security system with death certificates obtained from state health departments. Nearly all of the cohort has now been followed up to death.

Table 1 shows the follow up status of this cohort of workers in earlier reports and to the end of 1980. By 1980, 88% of the workers were known to be dead and for nearly all of these it was possible to locate a death certificate. Of the 130 presumed alive (table 1), 99 were verified as alive and 31 could not be located. For

Table 1 *Follow up status of male retirees from a United States asbestos company at different times*

	Follow up period		
Status	*1941–69*	*1941–73*	*1941–80*
Total of cohort:	1074	1074	1074
Dead:	617	782	944
Death certificate found	608	764	910
Death certificate not found	9	18	34
Presumed alive	457	292	130

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these 31, ages ranged from 78 to 97 at the end of 1980 so that none had reached an age when death would be almost certain.

The results shown in table 1 vary slightly from those previously published because, with continued follow up, some workers previously untraced were located whereas others previously known to be alive were lost. Also, one member of the earlier cohort was identified on the death certificate as a woman and the cause of death for one death was found to have been coded incorrectly.

Table 2 shows deaths by cause for the entire period from 1941 to 1980. Deaths were coded according to the seventh revision of the International Classification of Diseases; expected numbers of deaths are based on calendar age specific death rates for United States white men. When United States rates were coded according to revisions other than the seventh, comparability ratios were used to translate these to the seventh revision. Excesses or deficits in mortality are expressed as standardised mortality ratios (SMRs)—the ratio of observed deaths to

Table 2 *Observed and expected deaths and SMRs for 1074 retirees from a United States asbestos company by cause of death 1941–80*

Cause of death (7th revision codes)	*Obs*	*Exp*	*SMR*
All causes of death	944	762·77	123·8**
Tuberculosis (001–019)	14	4·47	313·1**
All malignant neoplasms (140–205)	208	129·87	160·2**
Buccal cavity & pharynx (140–148)	5	3·60	139·0
Digestive organs & peritoneum (150–159)	64	45·70	140·0*
Oesophagus (150)	4	2·95	135·6
Stomach (151)	20	11·09	180·4*
Large intestine (153)	14	14·24	98·3
Rectum (154)	9	5·66	159·0
Biliary passage & liver (155–156)	4	3·52	113·6
Pancreas (157)	8	7·37	108·6
All other digestive organs (residual)	5	0·87	571·4**
Respiratory system (160–164)	79	30·57	258·4**
Larynx (161)	2	1·75	114·1
Bronchus, trachea, lung (162–163)	77	28·44	270·7**
All other respiratory system (residual)	0	0·38	—
Prostate (177)	17	18·17	93·6
Testis & other male genital (178–179)	0	0·34	—
Kidney (180)	7	2·54	275·8*
Bladder & other urinary (181)	5	6·13	81·5
Malignant melanoma of skin (190)	0	1·74	—
Eye (192)	2	0·13	1544·5*
Central nervous system (193)	3	1·19	251·2
Thyroid gland (194)	0	0·28	—
Bone (196)	0	0·66	—
All lymphatic & haematopoietic tissue (200–205)	9	10·76	83·7
Lymphosarcoma, reticulosarcoma (200)	2	2·24	89·4
Hodgkins (201)	0	0·72	—
Leukaemia & aleukaemia (204)	3	5·36	56·0
All other lymphatic (202, 203, 205)	4	2·44	163·9
All other malignant neoplasms (residual)	17	8·06	210·9**
Benign neoplasms (210–239)	3	1·19	251·6
Diabetes mellitus (260)	15	11·62	129·0
Stroke (330–334)	85	92·00	92·4
All heart disease (400–443)	395	353·87	111·6*
Rheumatic heart disease (400–416)	6	4·11	146·0
Coronary heart disease (420)	315	280·80	112·2*
Hypertensive heart disease (440–443)	21	21·92	95·8
All other heart disease (residual)	53	47·04	112·7
Hypertension without heart disease (444–447)	7	4·96	141·2
Non-malignant respiratory disease (470–527)	86	49·35	174·3**
Influenza & pneumonia (480–493)	27	24·23	111·4
All other respiratory disease (residual)	59	25·12	234·9**
Asbestosis (523·2)	22	—	—
Ulcer of stomach & duodenum (540–541)	3	5·65	53·1
Cirrhosis of liver (581)	13	6·30	206·3*
Chronic nephritis (592)	2	4·23	47·3
All external causes of death (800–998)	22	24·82	88·6
Accidents (800–962)	16	18·95	84·4
Motor vehicle accidents (810–835)	6	6·30	95·2
All other accidents (residual)	10	12·65	79·1
Suicides (963, 970–979)	6	5·10	117·7
Homicides & all other (residual)	0	0·77	—
All other causes of death (residual)	57	74·44	76·6*
Unknown	34	—	—

*$p < 0.05$; **$p < 0.01$.

expected deaths × 100.

An excess in digestive cancer was noted in earlier reports. Table 2, however, shows that this was due largely to an excess in stomach cancer where the SMR was significantly raised. Respiratory cancer continues to be in excess as in previous reports. Of particular interest is the excess in kidney cancer not previously noted and an excess in cancer of the eye which, while based on only two deaths, is statistically significant. Death rates from tuberculosis and non-malignant respiratory disease are also high. The excess in non-malignant respiratory disease is largely due to deaths related to asbestos exposure; the reason for the excess in tuberculosis is not clear. Possibly there has been some diagnostic misclassification that has caused some asbestosis or other asbestos related lung conditions to be classified as tuberculosis. Overall death rates in this group of retired workers have been high and their exposure to asbestos has undoubtedly played an important part in this. Some additional data on the deaths shown in table 2 appear elsewhere.[5]

Of particular interest are the deaths due to malignant mesothelioma, a condition closely related to asbestos exposure. By the end of 1980 a total of eight cases could be identified from death certificates and are listed in table 3. These constitute slightly less than 1% of all deaths. At the time data for this study was collected the industrial hygienist assigned each worker to a principal department and a primary type of asbestos to which he had been exposed. Also, from exposure estimates for each job, it was possible to calculate a cumulative asbestos dust exposure for each death expressed as million particle per cubic foot years (mppcf-y). This formation is included in table 2.

Since the deaths from mesothelioma in table 3 are from a retired population it is not surprising that the latent period appears to be long—in one case 55 years. What is surprising, however, is that men dying from mesothelioma did not have an unusually high exposure to asbestos when compared with all retirees from the department to which they were primarily assigned. We can think of no explanation for this in view of other evidence showing a dose reponse relation between asbestos and mesothelioma.[6]

There is much evidence that peritoneal mesotheliomas are almost invariably associated with amphiboles rather than chrysotile asbestos.[7] The data in table 3 are not entirely inconsistent with this in view of the fact that, of the two men with peritoneal mesothelioma, one worked with insulation where exposure to amosite predominated and this was the only one of the eight deaths from mesothelioma with this type of exposure. On the other hand, there does appear to have been a peritoneal mesothelioma where the principal type of exposure to asbestos was to chrysotile. As in other studies, however, there is a possibility of exposure to more than one type of asbestos despite the fact that the worker's primary job may have involved only one particular type.

One question that might be asked of these data is whether the excess in respiratory cancer and the pattern of respiratory cancer reported previously continued to 1980. Table 4 compares the mortality pattern in relation to cumulative asbestos dust exposure at time of retirement for the periods 1941–69 and 1941–80. The fact that the dose response relations were similar for these two periods serves to validate the original observations. The relation for 1941–80 is shown in the figure with the linear regression equation that best describes the relation.

A second question that might be asked is whether the excess in respiratory cancer has been disappearing with the passage of time. This may be answered by examining the excess in various age groups and is shown in table 5. Apparently the SMR peaked 10 to 15 years after retirement but the numbers are small in the oldest age groups. Moreover, since the United States mortality data which formed a basis for calculating expected number of deaths is given only for the broad age group 85 and over, it is not certain that this is the correct rate for this retired population. Finally, the cause of death in the very old is often uncertain and their cause specific mortality rates may have little

Table 3 *Deaths from mesothelioma among 1074 retirees from a United States asbestos company. (Average exposure for retirees from this department in parentheses)*

Year of hire	*Age at hire*	*Year of death*	*Cumulative exposure (mppcf-y)*	*Principal department*	*Primary type of asbestos*	*Type of mesothelioma*	*7th revision ICD codes*
1920	36	1975	48	Textile (223)	Chrysotile	Peritoneal	227X
1926	40	1955	62	Maintenance (251)	Chrysotile	Pleural	212X
1928	27	1970	760	Cement shingle and sheets (255)	Chrysotile	Pleural	163·0
1929	26	1976	322	Textile (223)	Chrysotile	Pleural	162·1
1933	39	1972	140	Textile (223)	Chrysotile	Pleural*	163·0
1935	36	1973	210	Cement shingle and sheets (255)	Chrysotile	Unspecified	197·9
1936	44	1966	82	Insulation (305)	Amosite	Peritoneal	158·0
1941	44	1975	122	Cement pipe (230)	Crocidolite	Pleural	163X

*Possibly mesothelioma.

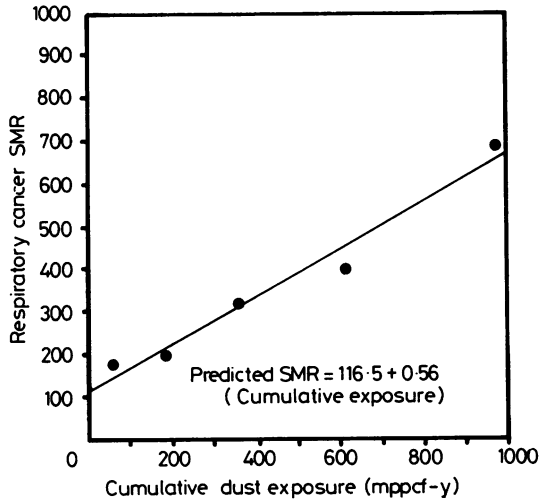
Table 4 *Observed deaths and SMRs for respiratory cancer for 1074 retirees from a United States asbestos company by total dust exposure*

Dust exposure (mppcf-y)	*Mean exposure (mppcf-y)*	*1941–69*		*1941–80*	
		Obs	*SMR*	*Obs*	*SMR*
Total	249	51	259·4**	79	258·4**
<125	62	16	194·7*	23	182·3*
125–249	182	7	172·5	14	203·1*
250–499	352	14	291·5**	24	322·0**
500–749	606	8	458·9**	10	405·0**
⩾750	976	6	714·8**	8	698·7**

*p < 0·05; **p < 0·01.

meaning.

A third question that might be asked of these data is, when did the excess in mortality begin to show up. Table 6 shows observed and expected deaths, SMRs, and excess death rates by time. Although follow up of the cohort of retirees started in 1941, no deaths from respiratory cancer were recorded until the period 1950–4. As noted earlier, retirees entered this cohort on their 65th birthday or at time of retirement if this came after age 65, thus the cohort was growing until 1967 after which no more new retirees were added. Table 6 shows that the SMRs remained relatively constant over a 31 year period whereas the absolute excess in death rates was increasing rather sharply. This reflects the fact that the background level of respiratory cancer was increasing in the United States at about the same rate as the death rates for respiratory cancer were increasing in this cohort and supports a notion presented earlier that asbestos effects multiply or are multiplied by whatever else it is in the environment that is responsible for respiratory cancer.[8] Thus it appears that when background rates are high, absolute excesses due to asbestos are also high.



Total asbestos dust exposure and respiratory cancer mortality, 1941–80.

Another observation from table 6 is that the excess in cancer among retirees might have been detected as early as 1960 when there had been a total of 12 deaths with only about five expected. Certainly by the end of 1964 the situation should have been clear. One interpretation that might be placed on this is that the United States asbestos company from which these workers retired should have been aware of the cancer problem at least by 1965 or perhaps earlier. The notion of mortality surveillance, however, which is now popular, was not widely applied before 1965 and the analytical methods used in this report would have been fairly complex for anyone then working in industry. The data in table 5 suggest, however, that monitoring of retired populations could be an extremely useful policy for large organisations where the possibility of a chronic disease hazard exists.

Table 5 *Observed and expected deaths and SMRs for respiratory cancer for 1074 retirees from a United States asbestos company by age, 1941–80*

Age	*No at risk*	*Person years*	*Observed*	*Expected*	*SMR*
65–69	1049	4573·9	22	9·86	223·2**
70–74	869	3592·8	25	9·86	253·6**
75–79	571	2187·5	28	7·05	397·1**
80–84	305	952·5	3	3·01	99·7
⩾85	101	333·6	1	0·80	125·3

**p < 0·01.

Table 6 *Observed and expected deaths, SMRs, and absolute risk for respiratory cancer for 1074 retirees from a United States asbestos company by year*

Year	*Person-years*	*Observed*	*Expected*	*SMR*	*Annual absolute risk (per/100 000)*
1950–54	1290·6	4	1·78	225·1	172·0
1955–59	1931·1	8	3·65	219·0	225·3
1960–64	2362·0	18	5·63	319·5**	523·7
1965–69	2590·0	21	7·91	265·6**	505·4
1970–73	1473·5	14	5·68	246·6**	564·6
1974–80	1211·1	14	5·24	267·2**	723·3

**$p < 0.01$.

Discussion

The large number of deaths now available make it possible to examine causes of death in more detail than before. Of particular interest is the excess in kidney cancer, an observation first made by others in 1979.[9 10] In the light of other reports this finding in retired asbestos workers may be important. The fact that the excess of digestive cancer was due largely to stomach cancer is also consistent with data from some other studies.[11 12] The two deaths due to eye cancer are of interest and have not to our knowledge been reported elsewhere. Whereas mortality from mesothelioma was not a striking feature of this cohort the fact that about 1% of deaths were due to mesothelioma is in keeping with other studies of workers primarily exposed to chrysotile asbestos. Doll and Peto have shown that for cohort studies of asbestos workers principally exposed to chrysotile asbestos 0·87% of the deaths were classified as mesothelioma.[7]

Some users of data from the cohort of retired asbestos workers have questioned the meaning of SMRs when follow up begins at age 65 as contrasted with follow up starting at time of job entry and have speculated that the slope of the dose response for respiratory cancer is underestimated in retirees because of deaths at earlier ages.[13] This could be the case if, for example, the Druckrey theory is correct—that is, response is primarily a function of time since first exposure so that nearly everyone would respond if enough time elapsed and competing causes of death did not intervene.[14] If this theory were true it would be manifest in a declining slope of the dose response curve with the passage of time. In a follow up to the end of 1973 we reported a regression of the data as: SMR = 100 + 0·66 (mppcf-y). In the present report to the end of 1980 the regression has changed to: SMR = 116·5 + 0·56 (mppcf-y). Thus as this population of retired workers aged, and the percentage of deaths moved from 60 to 88, the slope of the dose response relation diminished slightly—although perhaps not significantly.

Unfortunately, there are few studies of dose reponse relation that permit comparisons between percentage dead and dose response slopes. One such study was reported by McDonald *et al* in which they studied workers from an asbestos textile factory.[15] At the time of their study 34% of the population had died and they reported a regression of: SMR = 147·4 + 7·53 (mppcf-y). In an analysis of an earlier study of the same factory in which 26% of the population had died McDonald and his colleagues report a regression of: SMR = 161·5 + 11·14 (mppcf-y). The differences here could be related to the percentage of the cohort dead or to some other differences in the study populations. The slopes reported by McDonald *et al* are many times larger than the slope of 0·56 observed for retirees of whom 88% had died and the difference could be somehow related to the ages at which cohorts were followed up.

In addition to questions about the effects of age on dose response relations there is a related question as to whether workers who did not qualify for retirement had an unusual mortality experience. This is part of a more general problem in cohort analysis—that is, the effect of entering workers to follow up after they have had some work experience. The general issue here is whether the workers who leave before follow up begins have a different mortality experience than those who do not. There appears to be no answer to this; one study shows that early leavers have a higher mortality whereas another shows them having lower mortality.[16 17]

If the outcomes of cohort analysis are related to the ages at which the cohorts are followed up and if no single study is able to observe the outcomes at all ages, how should data be combined or selected to develop lifetime risk estimates? On the one hand, it would be unwise to depend heavily on studies of older workers if these understate dose response relations. On the other, since most deaths occur at older ages the experience of older populations is an important part of the concept of lifetime risk. Perhaps the first area for investigations should be to find out whether outcomes of cohort analyses are indeed related to ages at which cohorts are followed up.

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Clifford Sheckler, who in the 1960s classified every job in the asbestos operations of the Johns Manville Corporation in terms of the level of dustiness at various times. We also acknowledge the efforts of Hugh Jackson of the Johns Manville Corporation who helped in the first phase of this study and the work of Pierre DeCoufle who, as a student at the University of Pittsburgh, collected much of the demographic information on which this study was based.

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