

Latency of Asbestos Disease among Insulation Workers in the United States and Canada

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Two thousand two hundred seventy-one deaths were recorded among 17,800 asbestos insulation workers observed from January 1, 1967–December 31, 1976. There was little increase in cancer deaths or of asbestosis in less than 15–19 years from onset of employment. In general, though, the period of clinical latency was 2–4 decades or more and there were important differences among the several asbestos-associated diseases. Lung cancer peaked at about 30–35 years from onset and asbestosis at 40–45 years. Each tended to decline in incidence afterwards. Pleural and peritoneal mesothelioma reached their highest incidence later than lung cancer, but the incidence did not decline. In studies of effects of asbestos exposure, it appears advantageous to observe for at least 35–40 years or more from onset of exposure and to analyze the experience in duration-from-onset categories. If this is not possible, only the very limited early effects will be identified and the full import of the exposure may not be appreciated.

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ON JANUARY 1, 1967, the entire membership (17,800) of the asbestos workers union, International Association of Heat and Frost Insulators and Asbestos Workers, AFL-CIO, CLC, in the United States and Canada was registered. Observation has been maintained since, with the assistance of the approximately 120 local unions. Whenever an insulation worker associated with the union dies, we are notified. In most instances, a death certificate is forwarded; if not, it is obtained. Information is then sought concerning the details of the circumstances of death, including clinical data, roentgenograms, and histologic material obtained at surgery or autopsy. The clinical and roentgenological data are reviewed and the pathologic material examined. We have analyzed the mortality experience of the cohort in terms of underlying cause of death categorized according to best evidence available (BE), as well as by the underlying cause assigned on the basis of death certificate information only (DC).

At the onset of the study, a majority of the men were below the age of 40 (10, 101 of 17,800). The majority, too, had yet to achieve 20 years from first exposure (12,683 of 17,800) (Table 1). During the period January

1, 1967–December 31, 1976, the cohort changed its age and duration from onset distribution with the passage of time. Many of the men who started in the less than 20 years from onset group achieved 20 years from onset during the decade of observation (Table 2). Altogether, 12,683 men, with 89,462 man-years of experience, suffered 325 deaths in the period before 20 years. One thousand nine hundred and forty-six deaths occurred among 12,051 men who had achieved 20 years from onset, with 77,391 man-years of observation. The average age during observation was 36.3 years for the younger group and 53.8 years for those with longer duration from onset.

During the decade of observation, 1658.9 deaths were expected, based upon white male age-specific mortality data from the U. S. National Center for Health Statistics. Two thousand two hundred and seventy-one deaths occurred (Table 3). The excess deaths were primarily the result of an increased number of instances of cancer of several sites. Investigation of the deaths showed that 486 were due to bronchogenic carcinoma, between 4 and 5 times the number anticipated. There were 175 deaths of mesothelioma, 63 pleural in location and 112 peritoneal. There was a modest increase in deaths of gastrointestinal cancer (esophagus, stomach, colon-rectum).

Cancers of several other sites were also significantly increased over the number expected. There were 11 deaths from cancer of the larynx, 21 from the buccal cavity and oropharynx, as well as 19 deaths from cancer of the kidney. In each instance, this was twice the number of such deaths anticipated.

Review of the information concerning the deaths al-

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TABLE 1. Membership of Asbestos Insulation Workers' Union,* January 1, 1967, Classified by Age and Years from First Exposure to Asbestos Dust

Age	Total number of members	No. of years since first exposure to asbestos								
		0-9	10-14	15-19	20-24	25-29	30-34	35-39	40-49	50+
15-19	244	244								
20-24	1695	1695								
25-29	2412	2066	345	1						
30-34	2762	1065	1356	341						
35-39	2988	313	1141	1342	192					
40-44	2260	79	424	1026	591	139	1			
45-49	1589	49	131	433	442	487	47			
50-54	1297	27	88	214	332	377	182	77		
55-59	984	13	49	129	206	176	146	193	72	
60-64	703	1	21	59	131	126	87	99	179	
65-69	419	—	6	18	41	58	45	29	201	21
70-74	255	—	—	6	14	22	21	16	105	71
75-79	111	—	1	—	4	8	4	7	37	50
80-84	52	—	—	—	—	2	1	2	16	31
85+	29	—	—	—	—	—	—	2	7	20
TOTAL	17,800	5552	3562	3569	1953	1395	534	425	617	193

* Membership in the United States and Canada of the International

Association of Heat and Frost Insulators and Asbestos Workers, AFL-CIO, CLC.

lowed a distinction to be made between deaths caused by asbestosis and those of other noninfectious pulmonary diseases, including emphysema and cor pulmonale. One hundred sixty-eight deaths were assigned to asbestosis and 44 were attributed to other noninfectious pulmonary diseases, compared with a total expectation of 59.0 in the general population. The question of whether noninfectious pulmonary diseases, other than asbestosis, are or are not increased in asbestos workers, is a complex problem. Continuing questions of nomenclature of "chronic obstructive lung disease" in general and uncertainties of designation and pathologic cate-

gorization, were recently well reviewed by C. M. Fletcher.¹

Lapsed Period

It is now appreciated that most asbestos-associated disease is first seen after considerable periods from onset of exposure in both occupational and environmental circumstances. This is true both for the presence and extent of parenchymal fibrosis and pleural fibrosis and/or calcification^{3,4} and for asbestos-associated neoplasms.⁵

FIG. 1. Ratios of observed to expected deaths from lung cancer among 17,800 asbestos insulation workers observed prospectively 1967-1976, in five-year periods subsequent to onset of employment in this trade. The decline in ratios after the 30-35-year period may be the result of a "survivor-effect," since deaths associated with cigarette smoking (myocardial infarction, lung cancer, etc.) tend to selectively change the composition of the surviving cohort in relation to smoking status as time goes on.²

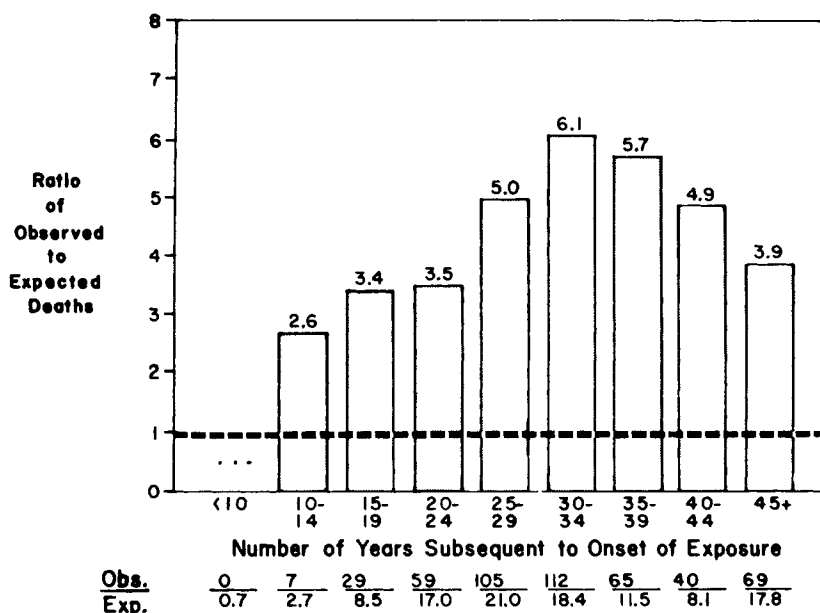


TABLE 2. Observation of 17,800 Asbestos Insulation Workers in the United States and Canada January 1, 1967–December 31, 1976

	Total	<20 years from onset	20+ years from onset
No. of men	17,800	12,683	12,051
Man-years of observation	166,855	88,464	7,391
Deaths	2,270	324	1,946
Average age during observation	44.4	36.3	53.8

Data obtained in this investigation now provide a more complete overview of this question. Broadly, we saw some limited excess disease in less than 20 years from onset of exposure (Table 4). Among 12,683 men with such experience, covering 89,462 man-years of observation, the number of cancer deaths was about

TABLE 3. Deaths among 17,800 Asbestos Insulation Workers in the United States and Canada January 1, 1967–December 31, 1976

Underlying cause of death	Expected*	Observed		Ratio o/e	
		(BE)	(DC)	(BE)	(DC)
Total deaths, all causes	1658.9	2271	2271	1.37	1.37
Total cancer, all sites	319.7	995	922	3.11	2.88
Cancer of lung	105.6	486	429	4.60	4.06
Pleural mesothelioma	†	63	25	—	—
Peritoneal mesothelioma	†	112	24	—	—
Mesothelioma, n.o.s.	†	0	55	—	—
Cancer of esophagus	7.1	18	18	2.53	2.53
Cancer of stomach	14.2	22	18	1.54	1.26
Cancer of colon-rectum	38.1	59	58	1.55	1.52
Cancer of larynx	4.7	11	9	2.34	1.91
Cancer of pharynx, buccal	10.1	21	16	2.08	1.59
Cancer of kidney	8.1	19	18	2.36	2.23
All other cancer	131.8	184	252	1.40	1.91
Non-infectious pulmonary diseases, total	59.0	212	188	3.59	3.19
Asbestosis	†	168	78	—	—
All other causes	1280.2	1064	1161	0.83	0.91

Number of men—17,800; Man-years of observation—166,853.

* Expected deaths are based upon white male age-specific U. S. death rates from the U. S. National Center for Health Statistics, 1967–1976.

† Rates are not available, but these have been rare causes of death in the general population.

(BE): Best evidence. Number of deaths categorized after review of best available information (autopsy, surgical, clinical).

(DC): Number of deaths as recorded from death certificate information only.

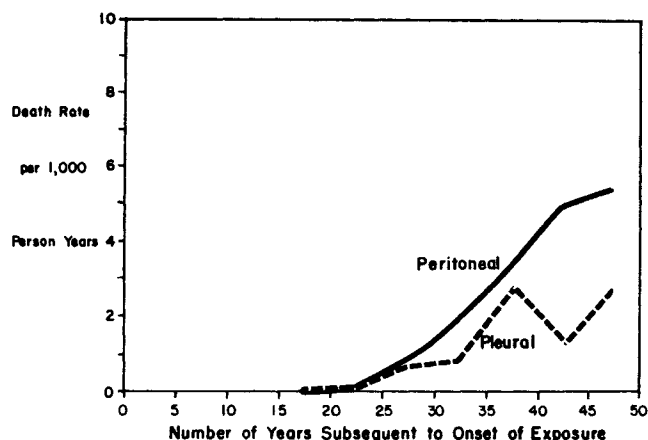


FIG. 2. Deaths per thousand person years of experience of pleural and peritoneal mesothelioma among 17,800 asbestos insulation workers from 1967–1976, analyzed by duration from onset of employment in five-year periods. Ratios between observed and expected deaths cannot be computed, since expected rates are not available for the general population. At least as of 45 years from onset, a decline in rates was not noted. This is consistent with the finding⁵ that cigarette smoking did not play a role in the risk of developing mesothelioma in contrast to lung cancer.

doubled, with 42.6 deaths expected and 83 observed. There were no excess deaths from gastrointestinal cancer and only five deaths from mesothelioma, with these in the category of 15–19 years from onset. Age, year, and sex-specific mortality data of the U. S. National Center for Health Statistics indicated that 11.9 deaths from lung cancer were to be expected. Thirty-six occurred. There were eight deaths from asbestosis.

On the other hand, extensive disease was seen among the 12,051 men who had reached 20 or more years from onset during the decade of study. Here, 1376.0 deaths were anticipated; 1946 occurred. There were 160 deaths from asbestosis and 912 from cancer. It was at this time that bronchogenic carcinoma made its heaviest contri-

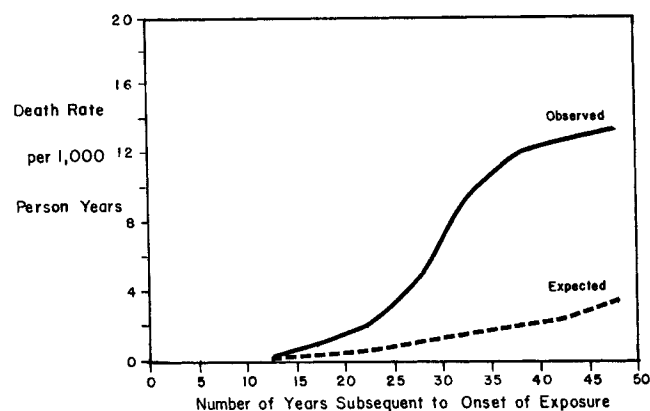


FIG. 3. To facilitate comparison with death rates for mesothelioma and asbestosis, death rates per thousand person years of lung cancer are shown, in five-year periods of duration from onset.

TABLE 4. Deaths among 17,800 Asbestos Insulation Workers in the United States and Canada January 1, 1967–December 31, 1976: Analysis by Duration from Onset of Employment

Underlying cause of death	Expected*	Before 20 years from onset 12,683 89,462				20 or more years from onset 12,051 77,391				
		Observed		Ratio o/e		Observed		Ratio o/e		
		(BE)	(DC)	(BE)	(DC)	(BE)	(DC)	(BE)	(DC)	
Total men										
Man-years of observation										
Total deaths, all causes	282.9	325	325	1.15	1.15	1,376.0	1,946	1,946	1.41	1.41
Cancer, all sites	42.6	83	77	1.95	1.81	277.1	912	845	3.29	3.05
Cancer of lung	11.9	36	32	3.03	2.69	93.7	450	397	4.80	4.24
Pleural mesothelioma	†	2	2	—	—	†	61	23	—	—
Peritoneal mesothelioma	†	3	0	—	—	†	109	24	—	—
Mesothelioma, n.o.s.	†	0	1	—	—	†	0	54	—	—
Cancer of esophagus	0.6	1	1	—	—	6.5	17	17	2.64	2.64
Cancer of stomach	1.5	1	0	—	—	12.7	21	18	1.65	1.42
Cancer of colon-rectum	4.1	4	4	—	—	34.0	55	54	1.62	1.59
Cancer of larynx	0.4	2	2	—	—	4.3	9	7	2.09	1.63
Cancer of pharynx	1.3	3	2	—	—	8.8	18	14	2.05	1.59
Cancer of kidney	1.1	3	3	—	—	7.0	16	15	2.29	2.14
All other cancer	21.7	28	30	1.29	1.38	110.1	156	222	1.42	2.02
Noninfectious pulmonary diseases, total	5.2	8	11	1.54	2.12	53.8	204	177	3.78	3.28
Asbestosis	†	8	2	—	—	†	160	76	—	—
All other causes	235.1	234	237	1.00	1.01	1,045.1	830	924	0.79	0.88

* Expected deaths are based upon white male age-specific U. S. death rates from the U. S. National Center for Health Statistics, 1967–1976.

† Rates are not available, but these have been rare causes of death in the general population.

(BE): Best evidence. Number of deaths categorized after review of best available information (autopsy, surgical, clinical).

(DC): Number of deaths as recorded from death certificate information only.

bution, with 93.7 such deaths expected and 450 observed. One hundred and seventy deaths from mesothelioma were then seen and the increase in gastrointestinal cancer found. Table 5 depicts these data in some detail, in five-year periods from onset of employment. Lung cancer data are given as both expected and observed numbers of death (Fig. 1). This practice cannot be followed for mesothelioma, where expected deaths

cannot be computed for the general population. Instead, we have provided data for both number of deaths of pleural and peritoneal mesothelioma as well as in terms of number of deaths of these causes per thousand persons-years at risk (Fig. 2). The latter does not take into account variations in achieved age, but this may have less influence than achieved duration from onset of employment. Major increases in numbers of deaths

TABLE 5. Deaths among 17,800 Asbestos Insulation Workers in United States and Canada, January 1, 1967–December 31, 1976: Analysis by Duration from Onset of Employment

Duration from onset (yrs)	No. of men	Person-years of observation	Lung cancer						Pleural mesothelioma		Peritoneal mesothelioma		
			Exp.*	Observed		Ratio o/e		No.		No./1000 person-years			
				(BE)	(DC)	(BE)	(DC)	(BE)	(DC)	(BE)	(DC)	(BE)	
<10	8,190	26,393	0.7	0	0	—	—	0	0	0	0	0	0
10–14	9,063	29,003	2.7	7	5	2.55	1.82	0	0	0	0	0	0
15–19	9,948	34,066	8.5	29	27	3.40	3.17	2	2	0.06	3	0	0.09
20–24	8,887	31,268	17.0	59	57	3.48	3.36	6	4	0.19	3	2	0.10
25–29	6,596	20,657	21.0	105	96	5.00	4.58	13	5	0.63	19	3	0.92
30–34	3,547	11,598	18.4	112	103	6.08	5.59	9	3	0.78	23	6	1.98
35–39	2,020	5,403	11.5	65	57	5.68	4.98	15	4	2.78	19	5	3.52
40–44	1,108	3,160	8.1	40	31	4.93	3.82	4	3	1.27	16	3	5.06
45+	1,448	5,305	17.8	69	53	3.89	2.98	14	4	2.64	29	5	5.47

* Expected deaths are based upon white male age-specific U. S. death rates of the U. S. National Center for Health Statistics, 1967–1976: Smoking habits not taken into account.

(BE): Best evidence. Number of deaths categorized after review

of best available information (autopsy, surgical, clinical).

(DC): Number of deaths as recorded from death certificate information only.

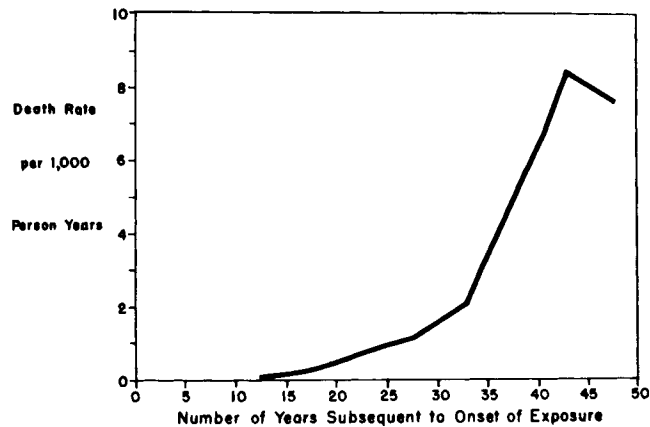


FIG. 4. Death rates of asbestosis among 17,800 asbestos insulation workers 1967–1976, analyzed in five-year periods of duration from onset of employment. Some decline is seen after 45 years from onset, possibly related to the added burden of smoking-induced lung disease superimposed upon asbestosis (at least in some cases^{5,6}) with selective survival of nonsmokers.

from lung cancer are first seen at 15–24 years from onset of work, with continued increases each decade (Fig. 3). The extraordinary increase in deaths from mesothelioma, both of the pleura and the peritoneum, is not observed until somewhat later, reaching 2.78 deaths per thousand persons-years at risk for pleural mesothelioma at 35–39 years from onset of work, and 5.47 deaths of peritoneal mesothelioma per thousand persons-years at 45 years from onset.

Summary

Little increase in cancer deaths, nor of asbestosis, was observed in less than 15–19 years from onset of exposure. In general, the period of latency between onset of exposure and death was two, three, four or more dec-

ades. Large increases in lung cancer occurred at 25–35 years from onset, but pleural and peritoneal mesothelioma showed their greatest incidence somewhat later. Under the conditions of exposure, the period of clinical latency for asbestosis was also prolonged (Fig. 4) and in many cases was 30–40 years or more from onset of employment. It appears that in studies of the effects of such asbestos exposure, it would be advantageous to analyze the experience of exposed individuals in duration-from-onset exposure categories, with particular reference to durations of more than 30 years. If this is not done, the risk is run of obscuring the neoplastic effects of asbestos exposure by the co-mingling of later deaths with those that may have occurred much earlier and could be much less likely influenced by asbestos exposure. In the same way, studies should include, whenever possible, the opportunity to observe the mortality of individuals at risk at least 30–35 and preferably 40 or more years from onset of their exposure. Again, unless this is possible, only the very limited early effects will be identified and the full import of the exposures may not be appreciated.

REFERENCES

1. Fletcher CM. Terminology in chronic obstructive lung diseases. *J Epidemiol Comm Health* 1978; 32:282–288.
2. Hammond EC, Selikoff IJ, Seidman H. Asbestos exposure, cigarette smoking and death rates. *Ann NY Acad Sci* 1979; 330:473–490.
3. Selikoff IJ, Churg J, Hammond EC. The occurrence of asbestosis among insulation workers in the United States. *Ann NY Acad Sci* 1965; 132:112–120.
4. Selikoff IJ. The occurrence of pleural calcification among asbestos insulation workers. *Ann NY Acad Sci* 1965; 132:351–367.
5. Selikoff IJ. Cancer risk of asbestos exposure. In: Hiatt HH, Watson JD, and Winston JA, eds. *Origins of Human Cancer*. Cold Spring Harbor, NY: 1977:1964–1984.
6. Selikoff IJ, Hammond EC. Asbestos and smoking. *JAMA* 1979; 242:458–459.