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MEDICAL RISKS

Trends in Mortality by Age and Time Elapsed

VOLUME 1

A Reference Volume Sponsored by
The Association of
Life Insurance Medical Directors of America
and The Society of Actuaries

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mixture of two metals makes it difficult to evaluate the effect of one or the other. Solvents not infrequently have similar neurotoxicity, and mixtures of solvents may lead to confusing observations.

Asbestos again provides a good example. After the first clinical case reports in the late 1920s, Merewether was asked by the Factory Inspectorate in Great Britain to investigate whether these cases were exceptions or pointed to a general problem. Merewether shied away from the construction industry, although most asbestos was used there, because many other exposures (cement, silica, wood dust, etc.) could have confounded the results. Rather, he observed workers in asbestos textile factories, where few other dusts occurred. Much disease was found; subsequent focus remained on "asbestos workers" in factories, rather than on much larger populations in industries where asbestos products were used.[9]

"Pure" exposures are the exception, not the rule. Concomitant or sequential multiple agent use is far more common because workers are employed in complex environments with multiple agent exposure. Indeed, not only are there multiple agents to be considered in the work environment, but the personal environment must also be taken into account, as indicated by the multiple factor interaction between asbestos and cigarette smoking,[10] benzene and radiation.

8. A particular kind of multiple agent exposure is seen in the mobility of employment during a worker's lifetime, with opportunity for multiple sequential exposures to potential hazardous agents. Unfortunately, in most occupational studies, lifetime occupational histories have been the exception rather than the rule, although this is changing. A few states require usual lifetime occupation to also be recorded on death certificates. Even the description of "last occupation" on death certificates cannot speak for the variety of exposures that could have occurred in a lifetime. My files contain a category for "Director's Disease." By the time an individual becomes a director of a corporation, he or she has often passed from the shop floor to industrial management to corporate management and, finally, to the director's suite, and has taken the effects of all exposures with him.

9. Diagnostic and Categorization Uncertainties

It is often difficult to fit "new" diseases into the previously established rigid categories of the International Classification of Diseases. This is true for the 6th to 8th revisions and, unfortunately, in the current 9th revision as well.

For decades, there was simply no place to put "mesothelioma" of the malignant variety seen in the pleura and peritoneal cavity. Even for well established neoplasms, inaccurate categorization exists, and comparisons among populations are often questionable.[11]

10. Industry Is Constantly Changing, with resulting secular changes in industrial agents and processes. The American Chemical Society has estimated that, in 1984, they were registering new chemicals at the rate of 70 *per hour*. While the vast majority do not enter commerce, at least several hundred do. One can wonder how the brave new world envisaged in the Toxic Substances Control Act will ever come into being, since preliminary laboratory investigation of potential hazard is most difficult, and epidemiologic data take years to accumulate.

In making quantitative projections for future estimates, it must be appreciated that current occupational exposures are generally much different from those in years past, being less intense and better controlled. Projections of future risk require great caution.

11. Reproductive Effects

We know very little about intrauterine exposures. Thalidomide and diethylsilbesterol sensitized us to this possibility, and experimental demonstration of transplacental angiosarcoma provided experimental data bearing on the matter. Nevertheless, as Tuchman-Dupleissis has ruefully commented, laboratory screening for adverse reproductive effects and birth defects has not lived up to the thalidomide promise.

Case Study: Asbestos-Associated Disease

Asbestos-associated cancer is now very much with us and is involved in a multitude of public health, industrial, legal, insurance, and clinical management problems. Yet these are due to an agent which was first found to cause fatal pulmonary fibrosis in 1899, in which parenchymal and pleural fibrosis was known to be common in the 1930s,[13] and where lung cancer was seen in 1935.[14] Additionally, a classic cohort study produced reliable epidemiologic evidence in 1955.[15]

Doll studied the mortality experience of 113 men who worked for a least 20 years in a "scheduled area" in an asbestos products factory during 1922-53. Some 0.8 deaths of lung cancer were anticipated and 11 were seen. He stated that, "From the data it can be concluded that lung cancer was a specific industrial hazard of certain asbestos workers among men . . . employed for 20 or more years . . ." This conclusion was entirely accurate. Yet when it is examined closely, one can appreciate how the constraints enumerated above limited the full characterization of the problem that could have warned of what lay ahead.

Doll investigated lung cancer. Yet, in retrospect, even with hindsight, one could not expect that the pan-[illegible] of other asbestos-associated neoplasms (mesothelioma, gastrointestinal cancer, oro-pharyngeal and laryngeal cancer, renal cancer) could have been seen as excessive in a study of 39 deaths among 113 people. Mesothelioma, for example, was not well established until 1960.[16] Doll did have one case of respiratory cancer categorized as "endothelioma of the pleura," but a single case was insufficient to warrant further special notice. (A single case is a weak signal.) Too, other neoplasms were present in some excess (2.3 expected, 4 observed). But with such limited experience one could not hope to evaluate whether or not a significant excess existed. This awaited a much larger cohort study. In one, for example, based on 166,853 man-years of observation, 2,271 deaths were analyzed (Table 4-2).[17]

Doll was very careful. He knew that changes in industry, in production techniques, and in conditions of potential exposure had occurred from the 1930s on. Therefore, he understood that he could only write about the past. Moreover, exposure measurements had not been made. The only population available to him for study were the men working in the "scheduled area" (government-designated as having heaviest exposures), and he could not provide information on what would happen to people who were associated with less intense exposure. We now know that later exposures in the same plant were, unfortunately, also associated with risk.[18]

Doll stated only what he knew. The workers whose experiences had been studied were employed in an asbestos products manufacturing factory.[13] Doll had no way of knowing that other asbestos-exposed workers, not studied by him, also had such risk; however, they did. Unfortunately, it turned out that for each worker manufacturing asbestos products, over a hundred were exposed with their use.[19] Doll could thus not tell us about shipyard workers, brake repair workers, family contacts, construction workers, and those exposed as a result of environmental circumstances. Doll spoke of exposure of "20 or more years." This was the result of a practical consideration: "... the labour in searching out the individual records of men employed for shorter periods would be disproportionately great ..." Thus, data concerning experiences of workers with shorter exposures — 1 month, 1 year, 10 years — followed for equally long periods of duration from onset of such exposure were unavailable to him. Yet we now know that such shorter exposure may be associated with a very substantial risk.[20] For asbestos, as for many agents, very many more workers are exposed for periods shorter than 20 years than are exposed for the longer term.

Finally, Doll did not have available to him the smoking histories of the men he studied, and he was unable to investigate the multiple factor interaction between asbestos exposure and cigarette smoking.[10] He was also unable to even consider, since this information was not included in the data made available to him, what might be the effect of asbestos brought home on workers' clothes. Newhouse and Thompson did not publish their study of mesothelioma among family contacts of asbestos workers until 1965,[21] and Anderson, et al., did not provide quantitative data in this regard until 1976.[22]

Considering the foregoing, it is sobering to realize that if asbestos had first been introduced in 1945 and Doll had investigated the experiences of workers in a plant of this new industry in 1975 or 1980, we might now be pointing to an equally excellent study establishing lung cancer as a risk of workers heavily exposed in a manufacturing plant. But we would know little or nothing about the full spectrum of asbestos neoplastic risk, the very large number of people who have been exposed in the use of the product, the augmentation of that risk by concomitant cigarette smoking, the problem of bystander exposure in shipyards and the construction industry, and we might conclude that asbestos accounted for very little of the cancer burden in the United States. Indeed, Doll would not have been able to make the estimate that 5% of all lung cancer in the United States was due to asbestos exposure.[23]

To complete this review, it is useful to report the current status of occupational disease derived from asbestos exposure during the period 1940 to 1979. This was studied by W. J. Nicholson and his colleagues[19] who investigated employment and asbestos exposure in important asbestos-using industries (mining and milling, primary manufacture of asbestos products, secondary manufacturing, shipbuilding and ship repair, insulation work, the construction industry, railroad engine repair (steam locomotives), utility services, stationary engineers and firemen, chemical plants and refineries, automobile maintenance, and merchant marine engine room personnel). Approximately 27.5 million new entrants joined these industries during the period. Some 32% had lesser intensity of exposure, and 68% had greater intensity. Taking into account such factors as likely duration of employment in each of the trades, "dose" (intensity x time) was considered. It was calculated that there were approximately 5,000 asbestos-related lung cancer deaths in 1982, and that this number would remain very much the same until the year 2000. For all asbestos-associated cancer in these

occupations and industries, 1982 saw a little over 8,000 deaths; it was projected that this would rise to nearly 10,000 by 1987 and then gradually decline over the next 20 years, provided there was no further asbestos exposure after 1980. These estimates did not include deaths of asbestos-associated cancer other than in the selected occupations and industries, since data were inadequate for such evaluations. Nor did they include deaths from asbestosis, nor disability from nonfatal asbestotic pulmonary and pleural changes.

Populations at Risk

The foregoing has been devoted primarily to calculations of deaths from asbestos. We are on much less firm ground concerning workers who have been exposed and may have the disease, but are not expected to suffer death. Of the 27.5 million individuals who, through 1979, had potential asbestos exposure at their work in the trades mentioned, 18.8 million had exposure in excess of the equivalent of two months employment as an insulator or asbestos factory worker. Some 21 million of the 27.5 million and 14.1 million of the 18.8 million were estimated to have been alive on January 1, 1980. These figures are given for those who reflect upon approaches to medical surveillance.

Costs of Asbestos-Associated Disease and Death

W. G. Johnson and E. Heler have provided calculations concerning the losses borne by workers or other survivors as a result of death and disability from exposure to asbestos.[24] They concluded that deaths between 1979 and 2027 would cost $309 billion, in addition to costs of medical care, litigation costs, and administrative costs incurred by social agencies, which costs were not included in the estimates. If to these amounts are added losses between 1967 and 1979, a total well in excess of $326 billion is reached. Parenthetically, pain and suffering of the workers and their families were considered not measurable. Disability compensation costs were also omitted, although such expenditures are expected to reach sums of many billions of dollars.

Calculations similar to the above have not been attempted for other occupational hazards.

Case Study: New York State

A different sort of analysis of the extent of occupational disease was recently undertaken for New York State,[25] using estimates that occupational exposures cause approximately 100,000 deaths and 400,000 new cases of acute and chronic disease annually in the United States, and that an estimated 2 million workers in the country are severely or partially disabled from occupational illnesses. Assuming that New York State generally suffers approximately one-tenth of all occupational diseases in the country, it was calculated that occupational exposures are responsible each year in New York State for 40,000 new cases of occupational diseases and 10,000 disease-related deaths, with an additional 200,000 workers in the state suffering from long-term disability due to occupational illness.

These estimates, admittedly crude, were made because there existed no comprehensive mechanisms either nationally or in New York State for the systematic collection of data on disease, disability, or death resulting from occupational causes. It was cautiously observed that, "It is quite possible, in fact, that the above figures underestimate substantially the full extent of the problem," since worker's compensation systems identified fewer than 5% of illnesses of occupational origin, and that the data collection systems mandated by the Occupational Safety and Health Administration identify fewer than 2% of occupational illnesses. It may also be noted that the Congressional Office of Technology Assessment recently concluded that, with so little agreement about the number of occupational illnesses, it refused to take a position about the "correct number."

Reviewing New York State industry, in addition to asbestos-associated disease a litany of occupational illnesses was listed: cancer of the bladder in dye workers, leukemia with benzene exposure, occupational bronchitis, disorders of the nervous system with solvent exposure, renal disease with lead, dementia and premature senility following chronic exposure to neurotoxins, heart disease in workers exposed to nitroglycerin and carbon monoxide, reproductive impairment with lead and a variety of pesticides, chronic repetitive trauma yielding diseases of the musculoskeletal system, noise-induced hearing loss, and skin cancer in workers exposed to coal tar pitch.

Insurance Experience

Mortality experience among men and women insured under group life insurance provides data for judging differences in mortality among actively employed persons by industrial groupings.[21] The 1970-79 experience indicated that the following industries recorded mortality at least 15% higher than the average for all industries combined.

References and Acknowledgments:

1. I. J. Selikoff, E. C. Hammond, and H. Seidman, "Mortality Experience of Insulation Workers in the United States and Canada, 1943-76," Ann. N.Y. Acad. Sci. 330 (1979): 91-116.
2. I. J. Selikoff, E. C. Hammond, and H. Seidman, "Latency of Asbestos Disease Among Insulation Workers in the United States and Canada," Cancer 46 (No. 12) (1980): 2736-40.

Subjects Studied:

(1) 632 members of two locals of the International Association of Heat and Frost Insulators and Asbestos Workers (the insulators union) in the New York - New Jersey metropolitan area who were registered January 1, 1943, as well as 833 members of these locals who joined the insulators union during the period January 1, 1943 to December 31, 1962, and had no prior asbestos employment before entering the union. Each group was studied separately.

On January 1, 1943, about half of the 632 members had been exposed to asbestos for 20 years or longer; almost all had had 10 or more years of exposure.

(2) 17,800 men on the rolls of the insulators union in the United States and Canada on January 1, 1967.

Follow-up: In the first study, 632 subjects were traced from January 1, 1943 to December 31, 1962, and then further from December 31, 1962 to December 31, 1976. The 833 subjects were traced from the date of joining the union to December 31, 1976.

In the second study, the 17,800 workers were traced from January 1, 1967 to December 31, 1976.

Clinical data, histological findings (on surgery or autopsy), and roentgenograms as well as information given on death certificates were used to determine causes of death.

Limitations of Studies: Information on smoking habits was not available. The experience for the most part covered a prolonged period of time during which many changes occurred in the handling of asbestos.

Mortality Results and Conclusions: Expected deaths for the two groups in the first study (632 and 833 subjects) were calculated on the basis of white male age-specific U.S. death rates for 1949-76; death rates for specific causes of death during 1943-48 were extrapolated from figures for 1949-76.

Expected deaths for the 17,800 subjects in the second study were calculated on the basis of white male age-specific U.S. death rates for 1967-76.

Study 1

An analysis of the mortality by years of exposure to asbestos, based on the experience among 632 New York and New Jersey asbestos insulation workers who had been working in the industry prior to January 1, 1943 and who were traced over the period January 1, 1943 through December 31, 1976, showed:

(a) Only 9 deaths among workers with less than 20 years of exposure to asbestos, or about the same as the number of expected deaths.

(b) 119 deaths among workers with 20-34 years of exposure to asbestos, resulting in a mortality ratio of about 150% for all causes of death. There were 53 deaths from all forms of cancer with a mortality ratio of nearly 400%, and 26 deaths from lung cancer with a mortality ratio of almost 900%. There were 7 deaths from mesothelioma and 3 deaths from asbestosis among these workers.

(c) 350 deaths among workers with 35 or more years of exposure to asbestos, resulting in a mortality ratio of about 150% for all causes of death. There were 155 deaths from all forms of cancer and a mortality ratio of about 370%, and 67 deaths from lung cancer with a mortality ratio of about 700%. There were 31 deaths from mesothelioma and 38 from asbestosis among these workers.

Clearly mesothelioma and asbestosis occurred only after a long period of time had elapsed following exposure to asbestos.

An analysis of the mortality by years of exposure to asbestos, based on the experience of 833 New York and New Jersey asbestos workers who began working after January 1, 1943 and were traced over the period from beginning of work to December 31, 1976, showed:

(a) Only 23 deaths among workers with less than 20 years of exposure to asbestos, or only about 60% of the expected deaths.

(b) 39 deaths among workers with 20-34 years of exposure to asbestos, resulting in a mortality ratio of about 160% for all causes of death. There were 15 deaths from all forms of cancer and a mortality ratio of about 300%. There were 3 deaths from mesothelioma and 6 deaths from asbestosis among these workers.

Study 2

An analysis of the mortality by years of exposure to asbestos, based on the experience of some 17,800 U.S. and Canadian asbestos workers over the period January 1, 1967 to December 31, 1976, showed:

(a) 325 deaths among workers with less than 20 years of exposure to asbestos, resulting in a mortality ratio of 115% for all causes of death. There were 83 deaths from all forms of cancer with a mortality ratio of about 200%, and 36 deaths from lung cancer with a mortality ratio of 300%. There were 5 deaths from mesothelioma, 8 from asbestosis, and 8 from non-infectious pulmonary disease among these workers.

(b) 1,946 deaths among workers with 20 or more years of exposure to asbestos, resulting in a mortality ratio of 141% for all causes of death. There were 912 deaths from all forms of cancer with a mortality ratio of 329%, and 450 deaths from lung cancer with a mortality ratio of 480%. There were also 204 deaths from non-infectious pulmonary disease with a mortality ratio of 379%. In addition, there were 170 deaths from mesothelioma and 160 deaths from asbestosis.

These findings confirm strongly the conclusion that very high mortality from mesothelioma, asbestosis, and non-infectious pulmonary disease occurs among asbestos workers after a long period of time (20 or more years) have elapsed following exposure to asbestos.

(c) Further analysis of lung cancer and mesothelioma mortality among the 17,800 asbestos insulation workers by time elapsed since beginning of employment including asbestos indicates that (i) lung cancer began to appear after about 10 years had elapsed; the mortality ratio from this cause rose to about 600% after 30-39 years from beginning of employment in the insulation industry; thereafter mortality ratios declined somewhat, and (ii) mesothelioma began to appear after 15 years had elapsed; the death rate from this cause rose steadily to more than 6 per 1000 after 35-44 years and to more than 8 per 1000 after 45 years from beginning of employment in the insulation industry.

TABLE 410A

ANALYSIS OF MORTALITY BY CAUSE ACCORDING TO DURATION OF EXPOSURE TO ASBESTOS
632 NY-NJ ASBESTOS INSULATION WORKERS JAN. 1, 1943 — DEC. 31, 1976

Cause of Death	LESS THAN 20 YEARS EXPOSURE TO ASBESTOS			20-34 YEARS EXPOSURE TO ASBESTOS			35 OR MORE YEARS EXPOSURE TO ASBESTOS			TOTAL		
	Deaths		Mortality	Deaths		Mortality	Deaths		Mortality	Deaths		Mortality
	Observed d	Expected* d'	Ratio* 100(d/d')	Observed d	Expected* d'	Ratio* 100(d/d')	Observed d	Expected* d'	Ratio* 100(d/d')	Observed d	Expected* d'	Ratio* 100(d/d')
All Causes	9	9.0	100%	119	80.4	148%	350	239.5	146%	478	328.9	145%
All Forms of Cancer	2	1.1	182	53	13.5	393	155	42.4	366	210	57.0	368
Cancer of Lung	0	0.2	0	26	3.0	867	67	10.1	663	93	13.3	699
Mesothelioma	0	NA	NA	7	NA	NA	31	NA	NA	38	NA	NA
Cancer of Esophagus, Stomach, Colon, and Rectum	0	0.03	0	13	3.8	342	30	11.0	273	43	15.1	285
All Other Cancer	2	0.6	333	7	6.7	104	27	21.3	127	36	28.6	126
Non-Infectious Pulmonary Disease	0	0.1	0	4	1.6	250	41	7.6	605	45	9.3	484
Asbestosis	0	NA	NA	3	NA	NA	38	NA	NA	41	NA	NA
All Other Causes	7	7.8	90	62	65.3	95	154	189.5	81	223	262.6	85

* Expected deaths calculated on white male age-specific U.S. death rates for 1949-76.

NA — Rare cause of death in general population; expected death rates not available.

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INSULATION WORKERS — U.S. AND CANADA

TABLE 4108

ANALYSIS OF MORTALITY BY CAUSE ACCORDING TO DURATION OF EXPOSURE TO ASBESTOS
833 NY-NJ ASBESTOS WORKERS JAN. 1, 1943 — DEC. 31, 1976

Cause of Death	LESS THAN 20 YEARS EXPOSURE TO ASBESTOS			20-34 YEARS EXPOSURE TO ASBESTOS			TOTAL		
	Deaths		Mortality	Deaths		Mortality	Deaths		Mortality
	Observed d	Expected* d'	Ratio* 100(d/d')	Observed d	Expected* d'	Ratio* 100(d/d')	Observed d	Expected* d'	Ratio* 100(d/d')
All Causes	23	39.8	58%	39	24.8	157%	62	64.6	96%
All Forms of Cancer	5	5.1	98	15	5.0	300	20	10.1	198
Cancer of Lung	2	1.1	182	8	1.8	444	10	2.9	345
Mesothelioma	0	NA	NA	3	NA	NA	3	NA	NA
Cancer of Esophagus, Stomach, Colon, and Rectum	1	0.7	143	2	0.8	250	3	1.5	200
All Other Cancer	2	3.3	61	2	2.4	83	4	5.7	70
Non-Infectious Pulmonary Disease	0	0.5	0	7	0.6	1,167	7	1.1	636
Asbestosis	0	NA	NA	6	NA	NA	6	NA	NA
All Other Causes	18	34.2	53	17	19.2	89	35	53.4	66

* Expected deaths calculated on white male age-specific U.S. death rates for 1949-76.

NA — Rare cause of death in general population; expected death rates not available.

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INSULATION WORKERS — U.S. AND CANADA

TABLE 410C

ANALYSIS OF MORTALITY BY CAUSE ACCORDING TO DURATION OF EXPOSURE SINCE EMPLOYMENT
17,800 U.S. AND CANADIAN ASBESTOS WORKERS JAN. 1, 1967 — DEC. 31, 1976

Cause of Death	LESS THAN 20 YEARS EXPOSURE TO ASBESTOS			20-34 YEARS EXPOSURE TO ASBESTOS			TOTAL		
	Deaths		Mortality	Deaths		Mortality	Deaths		Mortality
	Observed d	Expected* d'	Ratio* 100(d/d')	Observed d	Expected* d'	Ratio* 100(d/d')	Observed d	Expected* d'	Ratio* 100(d/d')
All Causes	325	282.9	115%	1,946	1,376.0	141%	2,271	1,658.9	137%
All Forms of Cancer	83	42.6	195	912	277.1	329	995	319.7	311
Cancer of Lung	36	11.9	303	450	93.7	480	486	105.6	460
Mesothelioma	5	NA	NA	170	NA	NA	175	NA	NA
Cancer of Esophagus, Stomach, Colon, and Rectum	6	6.2	97	93	53.2	175	99	59.4	167
All Other Cancer	36	24.5	147	199	130.2	153	235	154.7	152
Non-Infectious Pulmonary Disease	8	5.2	154	204	53.8	379	212	59.0	359
Asbestosis	8	NA	NA	160	NA	NA	168	NA	NA
All Other Causes	234	235.1	100	830	1,045.1	79	1,064	1,280.2	83

* Expected deaths calculated on white male age-specific U.S. death rates for 1967-76.

NA — Rare cause of death in general population; expected death rates not available.

‡ Number of observed deaths based on best evidence including autopsy, surgical, and clinical findings.

Source: Reference 1, Table 16 reproduced with permission of authors and publisher (New York Academy of Sciences).

INSULATION WORKERS — U.S. AND CANADA

TABLE 410D

ANALYSIS OF MORTALITY FROM LUNG CANCER AND MESOTHELIOMA ACCORDING TO DURATION OF EXPOSURE SINCE EMPLOYMENT 17,800 U.S. AND CANADIAN ASBESTOS WORKERS JAN. 1, 1967 — DEC. 31, 1976

Duration of Exposure Since Employment	Number of Men ℓ	Exposure E	Lung Cancer Deaths Observed† d	Lung Cancer Deaths Expected* d'	Lung Cancer Mortality Ratio* 100(d/d')	Mesothelioma Observed† Deaths d	Mesothelioma Death Rate per 1000 1000(d/E)
Less than 10 Years	8,190	26,393	0	0.7	0%	0	0.0
10-14	9,063	29,003	7	2.7	255	0	0.0
15-19	9,948	34,066	29	8.5	340	5	0.15
20-24	8,887	31,268	59	17.0	348	9	0.29
25-29	6,596	20,657	105	21.0	500	32	1.55
30-34	3,547	11,598	112	18.4	608	32	2.76
35-39	2,020	5,403	65	11.5	568	34	6.29
40-44	1,108	3,160	40	8.1	493	20	6.33
45 and Longer	1,448	5,305	69	17.8	389	43	8.11

* Expected deaths calculated on white male age-specific U.S. death rates for 1967-76.

† Number of observed deaths based on best evidence including autopsy, surgical, and clinical findings.

Source: Reference 1, Table 17 reproduced with permission of authors and publisher (New York Academy of Sciences).

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1. E. C. Hammond, I. J. Selikoff, and H. Seidman, "Asbestos Exposure, Cigarette Smoking and Death Rates," Ann. N.Y. Acad. Sci. 330 (1979): 473-90.
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3. H. Seidman and I. J. Selikoff, "Asbestos Exposure, Cigarette Smoking and Life Expectancy," Abstract, Proceedings of the International Symposium on the Prevention of Occupational Cancer, Helsinki, 21-24 April, 1981. Occupational Safety and Health Series, No. 46, p. 177, International Labor Office, Geneva.

Subjects Studied:

(1) 17,800 members of the International Association of Heat and Frost Insulators and Asbestos Workers alive on January 1, 1967, representing approximately 120 local unions in various parts of the United States and Canada, including Alaska and Hawaii; some 12,683 had fewer than 20 years of exposure to asbestos, and 12,051 had 20 years or more of exposure. The average age of the former was 36.3 and of the latter 53.8, with an average age of 44.4 for all of the subjects. In 1966 union members were asked to complete a questionnaire on smoking habits and use of protective masks.

The control group was selected from the American Cancer Society's Cancer Prevention Study launched in the fall of 1959. They comprised 73,763 white men who were not farmers, had no more than a high school education, had a history of occupational exposure to dust, fumes, vapors, gases, chemicals, or radiation, and were alive January 1, 1967. They were classified according to their smoking habits; age-specific death rates for each smoking classification were computed.

(2) 582 amosite asbestos factory workers who worked from June 1941 through December 1945 and were alive 20 years after beginning of employment (during 1961-65). Most of these men had a history of smoking.

(3) Same as in reference 1 — 17,800 members of the asbestos insulators union of whom 10,101 were under age 40 on January 1, 1967. Some 9,591 had a history of cigarette smoking at entry, and 1,457 had never smoked regularly.

Follow-up:

(1) Subjects traced from January 1, 1967 to December 31, 1976.

(2) Subjects traced from date they had 20 years of exposure to asbestos (during 1961-65) to December 31, 1977.

(3) Subjects traced from January 1, 1967 to January 1, 1980.

Limitations of Studies:

(1) The experience extended over a long period of time during which considerable change occurred in the handling of asbestos and in the smoking habits of the population (for instance reduced tar and nicotine content of cigarettes during the 1970s). Subjects and controls may have modified their smoking habits differently over the years.

(2) The factory in which the subjects worked was closed in 1954, so that for most of the subjects there was no further occupational exposure to asbestos thereafter.

(3) Same as for reference 1.

Mortality Results and Conclusions: Expected deaths in study 1 were calculated on the basis of age-specific death rates among the controls — men with the characteristics indicated selected from the American Cancer Society's Cancer Prevention Study, classified according to smoking habits.

Expected deaths in study 2 were calculated: (1) on the basis of age-specific death rates among New Jersey white males (1963-66, 1967-71, and 1972-77) without regard to smoking habits, and (2) on the basis of age- and smoking-specific death rates developed in the American Cancer Society's study for the controls selected in study 1.

Expected deaths in study 3 were calculated on the basis of age- and smoking-specific death rates in the American Cancer Society's study, extrapolated to January 1, 1980.

Causes of death in studies 1 and 2 were based on death certificates for the controls, but also on clinical and pathological reports for the subjects exposed to asbestos. This had to be done to identify the deaths attributable to mesothelioma and asbestosis.

(1) The first study showed that irrespective of smoking habits the men who had been exposed to asbestos dust for a least 20 years experienced mortality from all causes of about 170% of that in the control group; their relative mortality from cancer was about 350%, and from non-infectious pulmonary diseases about 300%. Their relative lung cancer death rate was about 550%, and their relative death rate from cancer of the larynx was about 360%.

There were 170 deaths (8.7%) from mesothelioma and 160 deaths from asbestosis (8.2%), based on the best available evidence.

The asbestos workers who smoked 20 or more cigarettes a day showed an overall (all causes) mortality ratio of about 200% in relation to asbestos workers who never smoked; their relative mortality from cancer of the lung was over 1,000% of that among nonsmokers.

Compared to the lung cancer death rates among the controls who never smoked, the asbestos workers who smoked 20 or more cigarettes a day recorded a mortality ratio of about 8,700%.

(2) The study of amosite asbestos factory workers who had been exposed to asbestos dust for at least 20 years indicated relative mortality from all causes of about 190% in relation to New Jersey death rates, but about 220% in relation to the mortality ratios in the control group. Their relative mortality from cancer was about 350% in relation to New Jersey cancer death rates, and about 390% in relation to the cancer death rates in the control group; their relative mortality ratios from lung cancer was about 600% in relation to both New Jersey and control group death rates from this cause. There were 14 deaths from mesothelioma (4.7%) and 18 deaths from asbestosis (6%) among them.

In relation to smoking habits, the amosite asbestos workers with a history of cigarette smoking recorded an overall (all causes) mortality ratio of about 210% compared to men with a matching history of smoking in the American Cancer Society's study, but a mortality ratio of about 375% in relation to nonsmokers. The corresponding figures for lung cancer were about 600% and 8,000%, respectively.

(3) This study of insulation workers showed that workers with a history of cigarette smoking experienced a relative mortality about 150% in relation to controls with similar smoking histories in the broad age range up to 80. Compared to controls who never smoked, the relative mortality was about 250% over a period of at least 40 years from the start of work with asbestos.

The study demonstrated clearly that cigarette smoking greatly increased the mortality of asbestos workers over a prolonged period.

ASBESTOS AND SMOKING

TABLE 411A

ANALYSIS OF MORTALITY BY CAUSE
EXPERIENCE 20 YEARS OR LONGER AFTER FIRST
OCCUPATIONAL EXPOSURE TO ASBESTOS DUST

Cause	Deaths		Mortality
	Observed[†] d	Expected[*] d'	Ratio[*,†] 100(d/d')
All Causes	1,946	1,148	170%
Cancer	912	259	352
Cardiovascular	566	660	86
Non-Infectious Pulmonary Disease	204	NA	NA
Asbestosis	160	NA	NA
All Other Causes	264	161	164
Lung Cancer	450	82	551
Mesothelioma	170	NA	NA
Colon-Rectum	55	31	181
Pancreas	21	16	131
Larynx, Buccal Cavity, and Pharynx	27	8	360
Stomach	21	13	168
Prostate	26	18	142

* Expected deaths based on experience of control group.

† Number of observed deaths based on best evidence including autopsy, surgical, and clinical findings.

NA — Rare cause of death in general population; expected death rates not available.

Source: Reference 1, Table 2 reproduced with permission of authors and publishers (New York Academy of Sciences).

TABLE 411B

ANALYSIS OF MORTALITY — TOTAL AND LUNG CANCER BY SMOKING HABITS EXPERIENCE 20 YEARS OR LONGER AFTER FIRST OCCUPATIONAL EXPOSURE TO ASBESTOS DUST

Smoking Habits	ALL CAUSES OF DEATH					LUNG CANCER				
		Expected Deaths*		Mortality Ratio*†			Expected Deaths*		Mortality Ratio*†	
	Observed†† Deaths	To All Asbestos Workers	To Men Who Never Smoked	To All Asbestos Workers	To Men Who Never Smoked	Observed†† Deaths	To All Asbestos Workers	To Men Who Never Smoked	To All Asbestos Workers	To Men Who Never Smoked
20 OR MORE CIGARETTES PER DAY										
Current	565	481.3	285.4	117%	198%	171	116.8	16.4	146%	1,040%
Ex Less Than 5 Years	166	137.5	81.8	121	203	54	33.3	4.7	162	1,151
Ex 5 to 9 Years	61	69.6	41.2	88	148	10	17.1	2.4	(58)	(415)
Ex 10 Years Plus	112	136.5	81.2	82	138	15	31.4	4.4	48	339
LESS THAN 20 CIGARETTES PER DAY										
Current	143	127.6	75.7	112%	189%	38	29.5	4.2	129%	915%
Ex Less Than 5 Years	22	20.0	11.9	110	185	5	4.8	0.7	(104)	(740)
Ex 5 to 9 Years	10	11.5	6.8	(87)	(146)	1	2.5	0.35	(—)	(—)
Ex 10 Years Plus	31	43.6	25.8	71	120	5	9.8	1.4	(51)	(362)
Pipe and Cigars Only	86	112.5	66.7	76	129	3	24.2	3.0	(—)	(—)
Never Smoked Regularly	94	158.2	158.0	59	100	5	35.5	5.0	(14)	(100)
Total (including unknown smoking habits)	1,946	1,946.0	1,158.3	100	168	450	450.0	63.4	100	710

* Expected deaths based on experience of control group.

† Where the number of deaths is 5 to 14, the mortality ratio is enclosed in parentheses. A dash (—) indicates fewer than 5 deaths.

†† Number of observed deaths based on best evidence including autopsy, surgical, and clinical findings.

Source: Reference 1, Table 6A reproduced with permission of authors and publisher (New York Academy of Sciences).

ASBESTOS AND SMOKING

TABLE 411C

ANALYSIS OF LUNG CANCER MORTALITY BY SMOKING HABITS EXPERIENCE 20 YEARS OR LONGER AFTER FIRST OCCUPATIONAL EXPOSURE TO ASBESTOS DUST

Smoking Habits	Deaths Observed d	Deaths Expected* d'	Mortality Ratio* 100(d/d')
Total With Known Smoking Habits	276	6.0	4,623%
History of Cigarettes	268	4.7	5,763
Current 20 or More Cigarettes Per Day	152	1.7	8,736
Current Less Than 20 Cigarettes Per Day	31	0.6	5,082
Ex Cigarettes	83	2.3	3,656
Pipe and Cigars Only	4	0.6	702
Never Smoked Regularly	4	0.7	533

* Expected deaths based on experience of control group.

Source: Reference 1, Table 7A reproduced with permission of authors and publisher (New York Academy of Sciences).

ASBESTOS AND SMOKING

TABLE 411D

ANALYSIS OF MORTALITY BY CAUSE† EXPERIENCE 20 YEARS OR LONGER AFTER FIRST OCCUPATIONAL EXPOSURE TO ASBESTOS DUST

Cause	Observed Deaths	Expected Deaths Based On NJ Death Rates	Expected Deaths Based On ACS Death Rates	Mortality Ratios Based On NJ Death Rates	Mortality Ratios Based On ACS Death Rates
All Causes	304	158.6	137.1	192%	222%
Cancer All Sites	116	33.4	29.8	347	389
Cancer:					
Lung	60	10.1	10.1	594	594
Mesothelioma	14	NA	NA	NA	NA
Larynx, Oral Cavity, and Pharynx	5	1.6	1.0	313	500
Colon-Rectum	11	5.2	3.7	212	297
Non-Infectious Pulmonary Disease	24	4.7	7.4	511	324
Asbestosis	18	NA	NA	NA	NA
Cardiovascular Diseases	122	95.3	81.2	128	150

† According to best evidence available.

NA — rare disease in general population; expected death rates not available.

Source: Reference 2, Table 4 reproduced with permission of authors.

ASBESTOS AND SMOKING

TABLE 411E

ANALYSIS OF ALL CAUSES MORTALITY BY SMOKING HABITS
EXPERIENCE 20 YEARS OR LONGER AFTER FIRST OCCUPATIONAL EXPOSURE TO ASBESTOS DUST

Smoking Habits	Observed Deaths	Expected Deaths		Mortality Ratios	
		Based On Men With Matching History of Smoking(ACS)	Based On Men Who Never Smoked Regularly(ACS)	Based On Men With Matching History of Smoking(ACS)	Based On Men Who Never Smoked Regularly(ACS)
History of Cigarette Smoking	214	102.3	56.7	209%	377%
Never Smoked Regularly	38	15.5	15.5	245	245
Pipe or Cigars Only	41	18.1	17.7	227	232
Smoking History Unknown	11	1.2	0.8	917	1,375
Total	304	137.1	90.7	222	336

Source: Reference 2, Table 6 reproduced with permission of authors.

ASBESTOS AND SMOKING

TABLE 411F

ANALYSIS OF LUNG CANCER[1] MORTALITY BY SMOKING HABITS
EXPERIENCE 20 YEARS OR LONGER AFTER FIRST OCCUPATIONAL EXPOSURE TO ASBESTOS DUST

Smoking Habits	Observed Deaths Lung Cancer[1]	Expected Deaths		Mortality Ratios	
		Based On Men With History of Smoking(ACS)	Based On Men Who Never Smoked Regularly(ACS)	Based On Men With History of Smoking(ACS)	Based On Men Who Never Smoked Regularly(ACS)
History of Cigarette Smoking	55	9.6	0.7	573%	7,858%
Never Smoked Regularly	3	0.2	0.2	1,500	1,500
Pipe or Cigars Only	2	0.2	0.2	1,000	1,000
Smoking History Unknown	0	0.1	0.0	0	0
Total	60	10.1	1.1	594	5,455

[1] According to best evidence available.

Source: Reference 2, Table 7 reproduced with permission of authors.

ASBESTOS AND SMOKING

TABLE 411G

ANALYSIS OF MORTALITY BY AGE AT START OF WORK WITH ASBESTOS BY SMOKING HABITS AND TIME ELAPSED

Years Elapsed From Start	Proportion Dead				Mortality Ratios			
	Insulation Workers		Controls		Insulation Workers Never Smoked Regularly (1) in Relation to (3)	Insulation Workers With History of Cigarette Smoking (2) in Relation to		
	Never Smoked Regularly	History of Cigarette Smoking	Never Smoked Regularly	History of Cigarette Smoking		(1)	(3)	(4)
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
AGES UNDER 25 AT START								
10	0.6%	1.3%	1.7%	1.8%	35%	217%	76%	72%
20	2.5	4.3	3.9	4.1	64	172	110	105
30	5.6	12.1	6.5	8.6	86	216	186	141
40	18.9	35.8	11.5	18.9	164	189	311	189
50	36.8	66.3	24.9	29.3	148	180	266	226
60	67.2	87.5	40.7	68.9	165	130	205	127
AGES 25-34 AT START								
10	2.1%	2.1%	2.0%	2.0%	111%	100%	105%	105%
20	3.2	6.0	4.7	6.0	70	188	128	100
30	7.9	21.0	9.0	15.1	90	266	233	139
40	26.1	52.2	20.4	33.6	126	200	256	155
50	50.7	71.6	44.9	63.3	118	141	159	113
AGES 35 AND OLDER AT START								
10		5.9%	3.4%	4.1%		174%	144%	
20		19.6	9.9	16.7		198	117	
30		47.0	23.5	37.5		200	125	
40		71.1	49.0	66.5		145	107	

Source: Adapted from Reference 3, Table 3.

CANCER
CHAPTER 5

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Nature of Cancer

Cancer is a generic term for a group of diseases characterized by a disorderly and uncontrolled growth of abnormal cells. Cancer cells, unlike normal cells, change and do not develop into useful tissues or organs. Cells of any tissue can become cancerous and retain some of their original structure.

At the beginning, cancer cells usually remain at their original site and the malignant tumor is said to be localized. Ordinarily, cancer cells do not stop multiplying once they start to do so. They may invade neighboring tissues or organs, constituting a local extension or infiltration.

Eventually some of the cancer cells enter a lymph channel or blood vessel and are carried to other parts of the body where they lodge and start secondary growths. This dissemination of malignant cells is called metastasis, and it is one of the reasons why cancer is so lethal. Metastasis may be confined to the region of the original site and is then termed regional, or it may spread to sites distant from the original one, in which case it is called distant or advanced.

Some cancers do not metastasize. We still do not understand what controls the multiplication and extension or infiltration of cells and tissues. The causes of many cancers are not known.

Cigarette smoking is estimated by the American Cancer Society to be responsible for 85% of lung cancer cases among men and 75% among women. The death rate of male cigarette smokers is more than double that of nonsmokers. Smoking has also been implicated in cancers of the mouth, pharynx, larynx, esophagus, pancreas, and bladder.

While it has been difficult to evaluate the role of alcohol by itself as a cause of cancer, consumption of alcoholic beverages is believed to increase the risk of cancer of the mouth, pharynx, and esophagus. The combined (synergistic) effect of alcohol and smoking has been easier to demonstrate.

Extensive research is under way to clarify the role of diet, nutrition, and food additives as cancer risks. Some studies suggest there may be a positive relationship with fat consumption and a negative relationship with fruit and vegetable consumption.

Other cancer risk factors include asbestos exposure, exposure to the drug diethylstilbestrol in utero, menopausal estrogen therapy, overexposure to the sun and other radiation, and exposure to many substances such as chromates, nickel, vinyl chloride, and others.

Dimensions of Cancer

During 1986 some 930,000 new cases of cancer will be diagnosed for the first time, and about 470,000 will die from it. On the average, 4 out of 10 cases diagnosed this year are expected to be alive 5 years hence. About 3 million Americans who were diagnosed and treated for cancer 5 or more years ago are living today without evidence of the disease.[1]

Table 5-1 indicates the importance of the major sites of cancer in 1986.

In 1986 the lung was the leading site of cancer among men — about 100,000 new cases — but in women the leading site of cancer was the breast, with nearly 125,000 new cases. In men cancer of the prostate, with 90,000 new cases, stood in second place, while in women cancer of the colon-rectum, with 73,000 new cases, was second. Ranking third among men was cancer of the colon-rectum (67,000 new cases), while cancer of the uterus (corpus and cervix combined with 50,000 new cases) was third in women.

The largest numbers of cancer deaths among men in 1986 were nearly 90,000 from lung cancer, 29,000 from colon-rectum cancer, and 26,000 from cancer of the prostate. Among women there were over 40,000 deaths from lung cancer, nearly 40,000 from cancer of the breast, and 31,000 from cancer of the colon-rectum.

Cancer is primarily a disease of older adults. The incidence of all forms of cancer in men aged 65 and older was four times that of men aged 45-64, while among women aged 65 and older the corresponding figure was 2½ times.[2] About 85% of all deaths from cancer occurred at ages 55 or older and ranked second only to the cardiovascular diseases as a cause of death in this age range.[3]