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ANALYSIS OF EXCESS LUNG CANCER RISK IN SHORT-TERM EMPLOYEES

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Lamm, S. H. (Consultants in Epidemiology and Occupational Health, Inc., Washington, DC 20007), M. S. Levine, J. A. Starr, and S. L. Tirey. Analysis of excess lung cancer risk in short-term employees. *Am J Epidemiol* 1988;127:1202–9.

An excess of lung cancer found in a cohort of 741 New York State tremolitic talc workers observed from 1947 through 1978 has been shown paradoxically to be concentrated in short-term workers. Review of past work histories suggests that the excess of lung cancer in these short-term workers may be accounted for by prior exposures rather than by exposures at the employment under investigation. This finding has significant implications in view of the developing practice of including short-term workers in occupational cohort studies in contrast to the more traditional practice of excluding short-term workers. The traditional practice was based on the assumption that the inclusion of short-term workers with little exposure, and thus little risk, might dilute an otherwise apparent association between mortality and exposure. This study suggests that in certain instances the inclusion of short-term workers may magnify rather than dilute the estimation of risk, reflecting the presence of confounding variables.

lung diseases; lung neoplasms; occupational diseases; talc

New York tremolitic talc workers have been the subject of numerous epidemiologic studies over the past 50 years. Early reports (1–4) focused on morbidity and mortality from pneumoconiosis and related pulmonary conditions. Excess cancer mortality was reported in 1967 and 1974 by Kleinfeld et al. (5, 6) in a proportional mortality study of 220 New York State talc miners and millers. Among 91 deaths, the only excess cancer mortality was for lung and pleural cancer. This excess was limited to those workers who had been hired prior to 1945 (at which time wet drilling industrial hygiene controls were introduced) and who had died prior to 1960 at age 60 years or greater.

In 1973, Kleinfeld et al. (7) examined 39 workers from an upper New York State talc plant which had begun operations in 1947 and had used only the modern wet drilling techniques. No malignancies, and only one case compatible with pneumoconiosis, were observed among these workers whose only known exposure to commercial talc was at the plant studied. The National Institute for Occupational Safety and Health (NIOSH) subsequently conducted industrial hygiene studies at this talc plant as well as undertaking cross-sectional morbidity and historical mortality studies of its

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Abbreviations: NIOSH, National Institute for Occupational Safety and Health; SMR, standardized mortality ratio.

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workers (8–10). From a cohort mortality study of 398 white males initially hired between January 1, 1947, and December 31, 1959, and followed for their vital status as of June 30, 1975, NIOSH reported finding a statistically significant excess mortality from lung cancer and from nonmalignant respiratory diseases.

An independent cohort mortality study of employees at this same talc plant was performed by Stille and Tabershaw (11). Their cohort study of the 655 white males employed between January 1, 1948, and December 31, 1977, assessed vital status as of December 31, 1978. They reported nonstatistically significant elevations of lung and respiratory cancer mortality in the total cohort and showed a significantly increased risk of respiratory cancers only for employees with any history of prior employment. The authors concluded that this increase was probably due to exposures that had occurred prior to employment at this talc plant.

Due to the conflicting findings with respect to excess mortality from lung cancer in this population of talc workers, a reanalysis of the data gathered by Stille and Tabershaw and by NIOSH has been undertaken.

Materials and Methods

Study population

The study population consisted of the cohort of 741 men and women who had ever worked at this talc plant from 1947, when the plant opened and began operations, through December 31, 1977. All of the employees in the study population were white. During this period, 705 men and 36 women had been hired. Mortality follow-up of the 36 women was conducted but not included in the statistical analysis because of the small numbers. A total of 425 men worked at the plant for one year or more; 280 worked for less than one year. The period of observation in the study extended from the date of hire to either the date of death, the date of loss to follow-up, or December 31, 1978, whichever date came first.

The data utilized for this analysis were originally collected by Tabershaw Occupational Medicine Associates as described previously (11). These data were abstracted from employment applications completed at the time of application for hire and from job cards and employment files maintained by the company. Death certificates were obtained by Tabershaw Occupational Medicine Associates and by NIOSH from state health departments. The cause of death was coded by nosologists using the *International Classification of Diseases*, Eighth Revision.

For this reanalysis, additional data on missing dates of birth for 16 workers were obtained from local hospital records. For the remaining 17 whose birth dates were missing from the records, an estimated birth date was developed by G. Block of the National Cancer Institute, using the method by Block et al. (12) based on the year of issuance of the social security number.

Prior employment history

Each prior employment experience indicated on the initial job application at this talc plant was categorized on the basis of its likelihood of association with an increased risk of lung cancer. This categorization was developed by a senior industrial hygienist without knowledge of the individual's vital status or cause of death. The basis for classification was as follows: "Lung cancer risk" jobs included metal mining (primarily lead/zinc mines) (13, 14), steel-making (15), foundry (16), roofing (17), welding (18), construction (19), and paper mill (20). Jobs such as retail sales and restaurant work were clearly classifiable as jobs with "no prior risk." Other employment categories, such as carpentry, electrical work, transportation, military, farming, and engineering, which are not clearly either at risk or free of risk were for this analysis also classified as "no prior risk" employment. Such a classification would tend to bias against finding a difference between the two risk classifications.

The previous analysis by Stille and Tabershaw (11) stratified only on the presence or absence of a prior work history on the job application, while our analysis stratifies on the basis of specific employment information contained in the prior work history.

Individual workers were then classified on the basis of the categorization of their prior employments as ever having had "prior risk" (353, or 50 per cent), as having "no prior risk" (214, or 30 per cent), or as "unclassifiable" (138, or 20 per cent) because their job application gave no indication of their prior work history.

Statistical methods

Observed-versus-expected deaths for all causes and for specific causes of deaths were developed and compared, using National Center for Health Statistics cause-specific death rates for US white males and using the analytic program developed by Monson (21) to calculate the expected numbers. Comparison between the observed and the expected number of deaths was expressed as a standardized mortality ratio (SMR), where SMR equals 100 times the observed deaths divided by the expected number of deaths.

Statistical significance of the difference of a standardized mortality ratio from 100 is presented as a two-tailed p value based on a Poisson distribution.

RESULTS

Mortality for the entire male cohort (table 1) was significantly elevated (SMR = 141) as were the risks of death from all cancers (SMR = 165), from the subclassifications of respiratory cancer (SMR = 246) and of lung cancer (SMR = 240), and from all nonneoplastic respiratory disease (SMR = 236). There was no significant excess mortality from nonrespiratory cancers. The recorded causes of the 10 nonneoplastic respiratory disease deaths were pneumonia (four), pneumoconiosis (two), emphysema (two) and other lung diseases (two). In addition, an electrician at the talc plant died from mesothelioma 15 years after being hired. He had previously worked 20 years in various employments as a miner, a miller, or in construction. Mortality for the 36 females revealed no deaths from lung cancer or other diseases of particular concern.

A similar analysis (table 1) was performed for the 425 men (60 per cent of the cohort) who had at least one year's duration of talc plant employment (experienced workers). The significantly increased mortality from lung cancer noted previously in the total group was no longer evident. The significant excess risk for all nonneoplastic respiratory diseases (SMR = 278) was seen to be restricted to deaths from noninfectious, nonneoplastic respiratory diseases (SMR = 370).

When mortality of the total cohort, of those employed for at least one year (i.e., one year or more), and of those employed for less than one year are compared for all causes, for all respiratory cancers, and for lung cancer (table 2), it becomes apparent that the excess mortality from lung cancer in this cohort is concentrated in those employees who were employed for less than one year. Furthermore, the excess mortality from noninfectious, nonneoplastic respiratory disease is found only in those who were employed for one year or more.

When prior exposure history is added to the analysis (table 3), it can be seen that lung cancer mortality risk also appears to be related to prior occupational exposures. Thus, lung cancer risk is found to be greater in those who had less than one year of employment in the talc plant, and seems to predominate in those who had potential lung cancer risk exposure prior to their talc employment.

In contrast to the findings for lung cancer mortality, mortality from noninfectious, nonneoplastic respiratory disease (table 4) is only demonstrable in those workers with one year or more of employment and, unlike lung cancer mortality, is not concentrated in employees with prior exposure risk.

The 12 cases of lung cancer observed in

TABLE I

Observed and expected numbers of deaths and standardized mortality ratios (SMRs) (1947–1978) among male upstate New York talc plant workers

Cause of death (ICD-8‡)	Deaths among all workers				Deaths among workers employed one year or more			
	Observed	Expected	SMR	CI†	Observed	Expected	SMR	95% CI
All deaths	118	83.6	141	117–166	61	49.8	126	97–157
Respiratory tuberculosis (010–019)	3	0.6	493	99–1438	2	0.4	576	65–2063
All cancer (140–209)	26	15.7	165	108–242	15	9.6	157	88–259
Digestive system (150–159)	5	4.2	119	39–278	2	2.5	80	10–288
Respiratory system (160–163)	13	5.3	246	131–420	7	3.3	213	85–438
Lung (162)	12	5.0	240	124–419	6	3.1	193	71–420
Genitourinary system (185–189)	2	1.7	118	14–425	2	1.0	202	24–729
Central nervous system (191)	1	0.6	161	2–898	1	0.4	262	3–1466
Lymphopoietic (200–209)	5	1.8	278	90–648	3	1.1	277	56–812
Other malignancies	0	2.3		0–174	0	1.2		0–308
Benign neoplasms (210–239)	1	0.3	309	5–2238	1	0.2	663	9–3718
Circulatory system (390–458)	52	39.5	132	98–168	30	23.4	129	87–183
All nonneoplastic respiratory disease (460–486)	10	4.2	236	113–435	7	2.5	278	111–572
Pneumonia (480–486)	4	1.6	252	68–644	1	0.9	109	1–605
Noninfectious, nonneoplastic respiratory disease (460–479 and 487–519)	6	2.6	227	83–495	6	1.6	370	135–806
Accidents (E800–949)	9	8.7	101	47–197	2	5.0	39	4–140
Other causes	17	14.6	116	68–186	6	8.8	68	25–149

† CI, confidence interval.

‡ *International Classification of Diseases*, Eighth Revision.

TABLE 2

All cause, respiratory cancer, lung cancer and noninfectious, nonneoplastic respiratory disease mortality risks (1947–1978) by duration of employment among male upstate New York talc plant workers

	Duration of employment					
	Less than one year		One year or more		Total cohort	
	Observed/ Expected	SMR†	Observed/ Expected	SMR	Observed/ Expected	SMR
All causes	55/33.8	163*	63/49.8	126	118/83.6	141*
Respiratory cancer	6/2.0	300*	7/3.3	213	13/5.3	246*
Lung cancer	6/1.9	317*	6/3.1	193	12/5.0	240*
Noninfectious, nonneoplastic respiratory disease	0/1.0		6/1.6	370*	6/2.6	227

* $p < 0.05$, two-tailed test.
† SMR, standardized mortality ratio.

TABLE 3

Lung cancer mortality risks (1947–1978) by duration of employment and prior exposure history among male upstate New York talc plant workers

Work history classification	Duration of employment					
	Less than one year		One year or more		Total cohort	
	Observed/ Expected	SMR†	Observed/ Expected	SMR	Observed/ Expected	SMR
Prior risk‡	3/0.9	333	6/2.0	308*	9/2.9	316*
No prior risk	1/0.4	286	0/0.5		1/0.9	117
Unclassifiable§	2/0.6	313	0/0.7		2/1.3	154
Total cohort	6/1.9	317*	6/3.1	193	12/5.0	240*

* $p < 0.05$, two-tailed test.
† SMR, standardized mortality ratio.
‡ Prior employment in job with lung cancer risk (see text).
§ No prior work history on job application (see text).

the total cohort are reviewed in table 5. Duration of employment of these workers varied from several days to over 17 years, with a mean of 4.7 years (median of 20 months). Ages at time of hire varied from 24 to 57 years, with a mean of 34.8 years (median of 32.5 years).

DISCUSSION

Inclusion of short-term workers in the analysis of occupational cohort studies is generally felt to dilute the measure of association of mortality with the exposure of interest because of minimal exposure duration. To compensate for this perceived difficulty, short-term employees are frequently omitted from the analysis.

We have presented an example of mortality from lung cancer occurring in an occupational cohort of talc workers which demonstrates an *increased* mortality confined precisely to those who are traditionally excluded from analysis, the employees with short-term exposure (less than one year). Risk from occupational exposures is generally expected to increase with duration of employment. Here the risk does not appear to do so. The paradoxical nature of this finding is emphasized by the contrasting fact that mortality from noninfectious, nonneoplastic respiratory disease in this cohort does follow the anticipated pattern of increased incidence with increased duration of employment.

When the lung cancer mortality is analyzed by duration of employment (table 2) and by prior exposure risk categories (table 3), it appears that the lung cancer mortality

TABLE 4

Noninfectious, nonneoplastic respiratory disease mortality risks (1947–1978) by duration of employment and by prior exposure history among male upstate New York talc plant workers

Work history classification	Duration of employment				
	Less than one year	One year or more		Total cohort	
	Observed/ Expected	Observed/ Expected	SMR†	Observed/ Expected	SMR
Prior risk‡	0/0.4	3/0.9	319	3/1.3	224
No prior risk	0/0.1	3/0.3	1200*	3/0.5	666*
Unclassifiable§	0/0.5	0/0.4		0/0.9	154
Total cohort	0/1.0	6/1.6	370*	6/2.6	227

* $p < 0.05$ two-tailed test.

† SMR, standardized mortality ratio.

‡ Prior employment in job with lung cancer risk (see text).

§ No prior work history on job application (see text).

TABLE 5

Characteristics of lung cancer deaths (1947–1978) among male upstate New York talc plant workers

Case no.	Duration of employment	Date of hire	Years of age at hire	Prior risk employment	Date of death
1	8.0 days	1948	57	Unclassifiable§	1970
2	19.0 days	1949	43	Unclassifiable§	1970
3	2.0 months	1948	31	None	1971
4	2.5 months	1948	26	Metal mining	1971
5	3.0 months	1948	24	Metal mining	1970
6	11.0 months	1948	34	Metal mining†	1973
7	2.5 years	1950	30	Metal mining	1974
8	2.8 years	1948	39	Metal mining	1964
9	3.8 years	1949	27	Metal mining	1961
10	12.0 years	1953	37	Paper mill‡	1975
11	16.8 years	1956	45	Metal mining, construction	1973
12	17.5 years	1952	25	Paper mill	1976

† Also 5 months employment at another talc mine.

‡ Also 12 years employment at another talc mine.

§ No prior work history on job application (see text).

is significantly increased for short-term employees (SMR = 317) but not for longer term employees (SMR = 193), and is significantly increased for those with prior risk employment (SMR = 316) but not for those whose prior work history indicates no such employment (SMR = 117).

Several factors might explain these findings, including significant exposures occurring prior to (or subsequent to) employment at this talc plant, greater exposures for those with the short period of employment at this talc plant, differences in smoking habits, or perhaps some other factors that distinguish the short-term employees.

Analysis of prior work histories as discussed above demonstrates that employment in industrial jobs associated with an increased lung cancer risk prior to employment at this talc plant may be significantly related to death from lung cancer. Little information on possible exposures after leaving this employment is available for evaluation.

It is possible that unusual working-conditions existed during the time of employment of the short-term workers, as opposed to that of employees who remained longer at the talc plant, but support of this possibility is not evident. It might be that work-

ers who stayed for a shorter time began with dustier jobs, but the distribution of initial job assignments was no different for those who left within one year than for those who remained employed for at least one year. The lung cancer mortality was found primarily among miners (nine of 12 cases) rather than millers, although measured exposures were greater for the millers. The risk of lung cancer did not appear strongly related to the date of hire. Five of the six deaths from lung cancer in short-term employees occurred in workers who had worked three or fewer months, with two having had, respectively, only eight and 19 days employment at this talc plant (table 5). The presence of unusual working conditions during these short employment time periods thus appears to be an unlikely explanation of our findings.

Variations in other potentially confounding variables in short-term workers, such as cigarette smoking habits, are also possible. Limited anecdotal information on these cases indicates that those who were known to be smokers were considered to be heavy smokers. Additional data collection might assess whether the smoking habit for these workers was greater than for comparison groups and whether the smoking habit of short-term workers differed from those of longer term workers.

Other sociobehavioral or environmental factors that affect subsequent cause and age of mortality may distinguish short-term employees from long-term employees. The "healthy worker effect" is usually applied to the distinction between the ever employed and the never employed or the general population (22). There may also be a "short-time employment effect" or a "very short time employment effect" on mortality patterns of workers. Gilbert (23) found in his Washington State study of nuclear plant employees that the greatest risks for cancer and noncancer mortality were among those employed less than two years. We found half the lung cancer deaths in our study of talc workers to be in those employed less than one year and one-third in those employed less than three months. Shindell et al. (24) found no differences in mortality risk by duration of employment in their study of chemical workers; however, their study was restricted to workers employed for three months or more. Further studies should be done to determine the differential mortality pattern of short-term or very short-term employees. The adverse health, behavior, or work-related practices of persons who remain at a specific company for only a short period of time may differ from the practices of those who remain for a longer period of time or those who were not hired. In this paper, our method has been to determine the vital status of all persons ever employed and then to analyse and assess the results by duration of employment.

Mortality from noninfectious, nonneoplastic respiratory disease was used as a surrogate measure of fibrogenic lung disease in this population. If the talc exposure experienced by workers at this plant is believed to be both fibrogenic and carcinogenic, one would expect a similar exposure-related mortality pattern for both lung cancer deaths and noninfectious, nonneoplastic respiratory disease. However, unlike lung cancer mortality, the mortality risk for noninfectious, nonneoplastic respiratory disease (table 4) is concentrated in those employees who worked more than one year (SMR = 370) and in those whose prior work history did not indicate prior risk (SMR = 666).

Analysis of the mortality risk by duration of employment reveals that the risk from lung cancer in this study decreased with duration of employment while the risk from noninfectious, nonneoplastic respiratory disease increased with duration of employment. This suggests that the sources of these risks are different.

Conclusions

The increase in lung cancer mortality observed in a cohort of talc workers has been shown to be concentrated in short-term employees. This increased lung cancer

risk in short-term workers is most likely due to risk acquired elsewhere, such as prior employments, or to differences in smoking experience or other behavioral characteristics. The inclusion of short-term employees in this occupational epidemiologic study has affected the apparent relation observed between exposure and outcome in a magnifying rather than a diluting manner. The analysis in this study suggests that the lung cancer risk demonstrated in this cohort may reflect risks acquired before this employment rather than during this employment. The assessment of risk by duration of employment can reveal unusual patterns that may indicate confounding variables.

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