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by [Liu Z](#), [Lee TS](#), [Kotek TJ](#)

Affiliation: Biological and Medical Research Division, Argonne National Laboratory, Illinois.

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Mortality among workers in a thorium-processing plant — a second follow-up

by Zhiyuan Liu, MD,^{1,2} Tze-San Lee, PhD,^{1,3} Thomas J Kotek, MS¹

LIU Z, LEE T-S, KOTEK TJ. Mortality among workers at a thorium-processing plant — a second follow-up. *Scand J Work Environ Health* 1992;18:162-8. A second follow-up of mortality was carried out for workers employed in a thorium-processing plant between 1915 and 1973. The study group comprised 3796 workers (3119 men and 677 women). Of the whole group, 926 (761 men and 165 women) were deceased and 2620 (2161 men and 459 women) were still alive, while 250 (6.6%) were lost to follow-up. For the male workers, the standardized mortality ratio (SMR) for all causes of death was 1.12 with a 95% confidence interval (95% CI) of 1.05-1.21. The SMR for the male workers was also significantly increased for all cancers (SMR 1.23, 95% CI 1.04-1.43) and lung cancer (SMR 1.36, 95% CI 1.02-1.78). For the female workers, the SMR was 0.74 (95% CI 0.63-0.86) for all causes and 0.53 (95% CI 0.35-0.78) for all cancers. The results of a Poisson regression analysis showed that there was no significant effect of the selected factors on lung cancer mortality.

Key terms: cancer, occupational cohort, Poisson regression analysis, radiation.

Thorium ores and purified thorium materials contain thorium-232, thorium-228, and varying amounts of their radioactive daughter products. Inhaled thorium and thoron daughter products can be considered potential health hazards from analogy with the known effects of radon daughters. The radioactive properties and biological behavior of thorium and its daughter products in humans have been reviewed by Rundo (1), and studies on the health effects of thorium exposure and body radioactivity of former thorium workers have been reported (2-7). The previous studies showed that high airborne concentrations of thorium-232, radon-220, and lead-212 were sometimes reached during plant operations and these high concentrations increased the tissue concentrations of thorium in workers at the thorium refinery.

A study of the mortality among the male workers of a thorium-processing plant through 1975 (some through 1976) has been reported (8, 9). The plant involved in thorium extraction was founded in 1902 and closed in 1973. The company originally manufactured incandescent mantles which required thorium nitrate as one of the raw materials. Thorium nitrate was imported from Germany in a refined state. When World War I eliminated that source of supply, the company

began its own processing of monazite sand to extract thorium. As the use of incandescent mantles declined with the widening use of electricity, the company developed refining processes for rare earth chemicals. During World War II, the company furnished thorium and rare earth products to a United States (US) government project, and for several years afterward it continued to supply them to the government. The present study extended the follow-up of male workers and first reports on the mortality of female workers employed in the plant. Poisson regression analysis was used to describe the joint effects of exposure factors on lung cancer mortality.

Subjects and methods

Study population

The study population, defined in detail in previous reports (8, 9), consisted of employees of a thorium-processing plant. The total number of workers identified from the company records was 4582. The cohort defined for this study was limited to all workers who worked in 1940 or later, including those hired earlier and still employed in 1940. The year 1940 was chosen because records of employees at the company prior to 1940 were incomplete. Workers with unknown social security numbers and year of birth or with unmatched social security numbers were excluded from the cohort. The present study was limited to analyses of 3796 (3119 male and 677 female) workers.

Exposure data

Information on work conditions and exposure to radioactivity at the thorium-processing plant was provided by the report of an industrial hygiene survey

¹ Environmental Health Section, Biological and Medical Research Division, Argonne National Laboratory, Argonne, Illinois, United States.

² Present address: Department of Epidemiology, UCLA School of Public Health, Los Angeles, California, United States.

³ On sabbatical from the Department of Mathematics, Western Illinois University, Macomb, Illinois, United States.

Reprint requests to: Dr Z Liu, Department of Epidemiology, UCLA School of Public Health, 10833 Le Conte Avenue, Los Angeles, CA 90024, USA.

made in 1952 (Klevin PB, Fresco J. "Lindsay Chemical Company Industrial Hygiene Survey: I Occupational Exposure to Thorium Dust and Thoron." US Atomic Energy Commission, New York Operation Office, Health and Safety Division, 21 January 1953, unpublished). However, no individual doses of radioactivity are available for the study population. Job classification and duration of employment were used to provide information relevant to thorium exposure. The daily estimated exposures of 84 male employees to thorium and thoron in 1952 by job classification were calculated from the data of Klevin & Fresco by Stehney et al (8). The jobs were classified into three groups. Group 1 (22 workers), including laborers and operators in the thorium extraction process, had the highest exposure to thorium (mean airborne alpha-particle activity concentration was 7.1 Bq). Group 2 (34 workers) included other laborers, foremen, maintenance and repair men, and superintendents. The range of the mean thorium exposure in this group was 0.9–2.0 Bq. Group 3 (28 workers), which had the lowest thorium exposure (0.1–0.5 Bq), included personnel in receiving, shipping, the control laboratory, offices, and others.

Vital status

The beginning and closing dates of the follow-up were 1 January 1940 and 31 December 1982, respectively. The vital status of the cohort was ascertained primarily through the Social Security Administration, and it was supplemented by use of company records, postal questionnaires, driver's license bureaus, and contacts with former co-workers. Of the 3796 workers, 761 men and 165 women were reported dead, 2161 men and 459 women were still employed or receiving payments and benefits, and 250 (6.6%) were lost to follow-up. The percentage traced was much improved as compared with that of the previous report (9). Among the male workers, a total of 250 deaths was added to the 511 deaths observed in the last study. All of the cohort members who were of unknown vital status were allowed to accumulate person-years in the study only until the date that they became unknown. For the 926 deaths, 864 (93.3%) death certificates were obtained. Causes of death, as reported on the death certificates, were coded by nosologists at the National Center for Health Statistics according to the "International Classification of Diseases, Adapted for Use in the United States," eighth revision (10).

Statistical analysis

Person-years of follow-up were accumulated for each subject beginning with either the year of first employment or 1940 and ending on the year of death, the date lost to follow-up, or the closing date of the study. The expected number of deaths was estimated with the computer program of Monson (11), which has been

updated to version 88 (1988). In the present report, US death rates for white males and females were used as the reference group in calculating the expected number of deaths because racial information was unavailable in the original records and there were only six (0.6%) blacks among the decedents. The standardized mortality ratio (SMR) was obtained by dividing the observed number by the expected number of deaths for each cause category. The 95% confidence interval (95% CI) of the SMR was computed with the method of Rothman & Boice (12).

The Poisson regression analysis (13–15) was used to describe the joint effects of exposure factors on lung cancer mortality. This multivariate analysis can take into account all study factors simultaneously and control time-related confounders. An internal comparison with the use of Poisson regression analysis was performed in which the model equation is in the form of "log (observed deaths) = log (person-years) + study factors + stratification factors." A Poisson regression model was fitted with the use of the generalized linear interactive modeling (GLIM) package (16). In the context of maximum likelihood estimation, the overall discordance between the predictions of a model and the observed data can be measured by "deviance," which is twice the difference between the log-likelihood of the present model and a completely saturated model. The deviance is distributed asymptotically as the chi square with degrees of freedom equal to the number of cells having nonzero person-years of observation minus the number of independent parameters in the model. When the value of the deviance exceeds its degrees of freedom by an amount significantly greater than expected under chi-square sampling, we concluded that the fit was inadequate.

The following three study factors were selected for the Poisson regression analyses: job classification (2 levels: group 1 and groups 2 and 3 as described), duration of employment (3 levels: ≤ 1 , 2–12, and ≥ 13 months), and time since first employment (3 levels: < 15 , 15–29, and ≥ 30 years). The two stratification factors were age and calendar year at follow-up. Both were divided into four intervals. Of 288 possible cells ($2 \times 3 \times 3 \times 4 \times 4$), 186 cells with nonzero person-years were used for the internal analysis of lung cancer.

Results

The numbers of deaths observed and expected and the SMR values of the male workers, by cause of death, are shown in table 1. The overall SMR was 1.12, which was statistically significant with a 95% CI of 1.05–1.21. The overall SMR of 1.12 was greater than that in the earlier report (SMR 1.05), which was not significant (95% CI 0.96–1.15). The SMR values of all the malignant neoplasms (SMR 1.23, 95% CI 1.04–1.43) and lung cancer (SMR 1.36, 95% CI 1.02–1.78) were similar to those in the earlier report, but they were

Table 1. Observed and expected deaths among 3119 male thorium workers and the standardized mortality ratios.^a

Selected causes of death ^b	Observed deaths (N)	Expected deaths (N)	Standardized mortality ratio	95% confidence interval
All malignant neoplasms (140—209)	158	128.72	1.23	1.04—1.43
Buccal cavity, pharynx	4	4.07	0.98	0.26—2.52
Digestive organs, peritoneum (150—159)	42	36.79	1.14	0.82—1.54
Stomach (151)	10	7.48	1.34	0.64—2.46
Large intestine (153)	11	11.66	0.94	0.47—1.69
Rectum (154)	7	4.10	1.71	0.68—3.51
Pancreas (157)	10	6.79	1.47	0.70—2.71
Respiratory system (160—163)	56	41.26	1.36	1.03—1.76
Lung (162)	53	38.95	1.36	1.02—1.78
Bone (170)	2	0.71	2.83	0.32—10.21
Prostate (185)	11	8.94	1.23	0.61—2.20
Brain, central nervous system (191—192)	3	4.03	0.75	0.15—2.18
Lymphosarcoma, reticulosarcoma (200)	3	2.62	1.14	0.23—3.34
Hodgkin's disease (201)	3	1.83	1.64	0.33—4.79
Leukemia, aleukemia (204—207)	6	5.41	1.11	0.40—2.41
Diseases of blood and blood-forming organs (280—289)	—	1.74	0	.
Circulatory diseases (390—458)	325	339.47	0.96	0.86—1.07
Respiratory diseases (460—519)	45	37.71	1.19	0.87—1.60
Pneumonia (480—486)	16	14.85	1.08	0.62—1.75
Emphysema (492)	13	7.91	1.64	0.87—2.81
Asthma (493)	1	1.45	0.69	0.01—3.83
Digestive diseases (520—577)	33	32.36	1.02	0.70—1.43
Genitourinary diseases (580—629)	10	11.34	0.88	0.42—1.62
External causes (800—998)	111	81.02	1.37	1.13—1.65
All accidents (800—949)	89	56.02	1.59	1.28—1.96
Motor vehicle accidents (810—827)	55	27.56	2.00	1.50—2.60
Suicide (950—959)	13	17.53	0.74	0.39—1.27
Unknown cause	43	.	.	.
All causes (000—999)	761	677.22	1.12	1.05—1.21

^a Total person-years of follow-up = 71 982, average age at entry = 29.73 years, average year at entry = 1956.2.^b Code of the International Classification of Diseases Adapted for Use in the United States (eighth revision) (10) in parentheses.

significant in this study due to the extension of the follow-up. For several other cancer sites, the SMR values were greater than 1.00, but none was statistically significant. The external causes, mainly due to motor vehicle accidents, still showed a significantly increased SMR (SMR 1.37, 95% CI 1.13—1.65). The SMR for diseases of the circulatory system (SMR 0.96, 95% CI 0.86—1.07) was different from that in the earlier report, which, at 0.82 (95% CI 0.71—0.94), was significantly less than 1.00.

The numbers of observed and expected deaths and the SMR values of the female workers are shown in table 2. The overall SMR was 0.74, which was statistically significant with a 95% confidence interval of 0.63—0.86. The SMR values for all cancers and circulatory diseases were also significantly below 1.00. There were slight, but not significant, increases in observed over expected deaths from lung cancer and digestive diseases. Because of the small sample size, no further analysis was performed for the female workers.

Table 3 shows variations of the SMR values for all malignant neoplasms and lung cancer among the male

workers according to selected study factors. Because 120 workers were of unknown status for job classification or duration of employment, only 2999 of the 3119 men were used for this analysis and the subsequent Poisson regression analysis. No conspicuous variations in the SMR values for all malignant neoplasms and lung cancer were observed for the male workers with these selected factors.

Table 4 presents the regression coefficients and associated relative risks of the Poisson regression model fitted to data on lung cancer according to the three study factors. The result of the goodness-of-fit statistics (deviance 116.27, degrees of freedom 174) of the main-effects model for lung cancer suggested that the assumption of the Poisson model was valid. The changes in the deviances for each of the factors showed that none of them had a significant effect on the mortality from lung cancer. Since none of the tests for the two-factor interactions (not shown in table 4) were significant, the simple multiplicative model should provide a reasonable description of the data. The relative risks in table 4 are exponentiated regression coefficients. None of the relative risks for lung cancer were

Table 2. Observed and expected deaths among 677 female thorium workers and the standardized mortality ratios.^a

Selected causes of death ^b	Observed deaths (N)	Expected deaths (N)	Standardized mortality ratio	95% confidence interval
All infective and parasitic (000—139)	2	2.90	0.69	0.08—2.49
All malignant neoplasms (140—209)	26	48.89	0.53	0.35—0.78
Digestive organs, peritoneum (150—159)	3	14.15	0.21	0.04—0.62
Liver (155—156)	—	1.46	0	—
Pancreas (157)	—	2.31	0	—
Respiratory system (160—163)	5	4.71	1.05	0.34—2.46
Lung (162)	5	4.53	1.10	0.36—2.58
Bone (170)	—	0.21	0	—
Breast (174)	5	10.04	0.50	0.16—1.16
Uterus (180—182)	3	4.53	0.66	0.13—1.94
Genital organs (180—184)	6	8.01	0.75	0.27—1.63
Leukemia, aleukemia (204—207)	1	1.69	0.59	0.01—3.29
Diseases of blood and blood-forming organs (280—289)	—	0.81	0	—
Circulatory diseases (390—458)	82	123.89	0.66	0.53—0.82
Respiratory diseases (460—519)	7	10.36	0.68	0.27—1.39
Digestive diseases (520—577)	9	8.59	1.05	0.48—1.99
External causes (800—998)	8	9.47	0.84	0.36—1.66
Unknown cause	19	—	—	—
All causes (000—999)	165	224.21	0.74	0.63—0.86

^a Total person-years of follow-up = 21 468, average age at entry = 31.83 years, average year at entry = 1947.8.^b Code of the International Classification of Diseases Adapted for Use in the United States (10) in parentheses.**Table 3.** Standardized mortality ratios for all malignant neoplasms and lung cancer among the male thorium workers according to selected study factors.

Study factors	All cancers			Lung cancer		
	Deaths (N)	Standardized mortality ratio	95% confidence interval	Deaths (N)	Standardized mortality ratio	95% confidence interval
Job classification ^a						
Group 1	113	1.23	1.01—1.47	39	1.38	0.98—1.89
Group 2	19	1.44	0.86—2.24	6	1.37	0.50—2.99
Group 3	21	1.28	0.79—1.96	5	1.12	0.36—2.62
Duration of employment						
≤ 1 month	55	1.38	1.04—1.80	22	1.80	1.13—2.73
2—12 months	44	0.99	0.72—1.33	15	1.10	0.62—1.81
≥ 13 months	54	1.44	1.08—1.88	13	1.16	0.62—1.99
Time since first employment						
< 15 years	57	1.40	1.06—1.82	17	1.73	1.01—2.77
15—29 years	67	1.21	0.94—1.54	21	1.17	0.73—1.80
≥ 30 years	29	1.12	0.75—1.61	12	1.29	0.67—2.25
Year at first employment						
1915—1954	115	1.27	1.05—1.53	33	1.24	0.85—1.74
1955—1973	38	1.21	0.85—1.65	17	1.65	0.96—2.64
Age at first employment						
< 20 years	7	0.85	0.34—1.75	3	1.16	0.23—3.39
20—29 years	25	0.97	0.63—1.43	7	0.81	0.33—1.67
≥ 30 years	121	1.38	1.15—1.65	40	1.55	1.11—2.11
All cohort	153	1.26	1.07—1.47	50	1.35	1.00—1.78

^a Group 1 includes laborers and operators in the thorium extraction process; group 2 includes other laborers, foremen, maintenance and repair men, and superintendents; group 3 includes personnel of receiving, shipping, control laboratory, office, and others.

statistically significant. No dose-response relationships of lung cancer risk with duration of employment or time since first employment were observed in the results of the Poisson regression analysis.

Discussion

This study extends the follow-up of male workers (8, 9) and first reports on the mortality of female

Table 4. Regression coefficients and related relative risks of the Poisson regression model fitted to data on lung cancer among the male thorium workers.^a

Factors	Coefficient	SE	Relative risk
Job classification ^b			
Group 2 + 3	.	.	1.00
Group 1	0.038	0.357	1.04
Duration of employment			
≤1 month	.	.	1.00
2—12 months	-0.453	0.337	0.64
≥13 months	-0.348	0.358	0.71
Time since first employment			
<15 years	.	.	1.00
15—29 years	-0.194	0.381	0.82
≥30 years	-0.126	0.470	0.88
Deviance ^c	116.27	(174)	

^a Adjusted for age at follow-up (4 levels: <45, 45—54, 55—64 and ≥65 years) and year at follow-up (4 periods: 1940—1949, 1950—1959, 1960—1969 and 1970—1982).

^b Group 1 includes laborers and operators in the thorium extraction process; group 2 includes other laborers, foremen, maintenance and repair men, and superintendents; group 3 includes personnel of receiving, shipping, control laboratory, office, and others.

^c Degrees of freedom in parentheses.

workers employed in a thorium-processing plant. The present search of the Social Security Administration records resulted in a small change in the sample size of the cohort, and intensified follow-up efforts improved the vital status ascertainment. The number of deaths among the male workers increased from 511 to 761. Both traditional SMR analysis and multivariate analysis (Poisson regression analysis) were used.

The SMR analysis has long been employed as a principal method of cohort studies (17—18). An advantage of the SMR analysis is that it can provide a mortality picture of the age- and time-specific observation period for any particular subgroup and may help to identify particular causes of death for further detailed analysis. However, the SMR analysis has also been recognized as having the serious problem of “noncomparability” between a study population and a reference population (19—22). The result of the SMR analysis should be interpreted with caution. In recent years, statistical methods for an internal comparison within a cohort and multivariate analysis have been developed for cohort analysis (13).

In the present study, an increased overall mortality was observed among the male workers. The SMR value for all causes among the male workers was 1.05 (95% CI 0.96—1.15) in the earlier study and 1.12 (95% CI 1.05—1.21) in the present one. Although much of the excess mortality could be attributed to nonoccupational motor vehicle accidents (SMR 2.00, 95% CI 1.50—2.60), the SMR was also significantly increased for all malignant neoplasms (SMR 1.23, 95% CI 1.04—1.43) and lung cancer (SMR 1.36, 95% CI 1.02—1.78), and it was increased, although not sig-

nificantly so, for most other cancers and respiratory diseases.

Several studies on health effects in populations occupationally exposed to radiation have been published (23—26). Beral et al (27) reviewed eight cohort studies which included the experience of 120 000 workers in the nuclear industry and concluded that no major health hazard associated with work in the nuclear industry could be identified. For the entire work force, overall mortality rates were below their respective national rates. Beral et al noted that this finding was consistent with the relatively high social classes of the employees and the initial selection of healthy persons into the work force. By combining data collected at a US commercial nuclear power plant with records from the Nuclear Regulatory Commission, Goldsmith et al (28) found no evidence of excess mortality among the plant employees. In the latest study at the Hanford site (23), Gilbert et al concluded that Hanford workers continued to exhibit a strong healthy worker effect with death rates substantially below those of the US general population. However, other investigators have reported an increased risk of cancers for Hanford workers (24, 29—32). A mortality study among a cohort of World War II nuclear industry workers at Oak Ridge also showed significantly increased SMR values for all causes (SMR 1.11), lung cancer (SMR 1.27), and respiratory diseases (SMR 1.25) (25).

The results for the female workers showed little evidence of adverse health effects. Their SMR values for all causes (SMR 0.74), all cancers (SMR 0.53), and circulatory diseases (SMR 0.66) were all significantly below those of the general US female population. These low SMR values were generally consistent with results reported in other studies of workers who have been exposed occupationally to low levels of external radiation (23, 26—28, 33—34). The healthy worker effect might be one of the reasons for the low SMR values. It is unclear if there is any preventive effect from low levels of external radiation.

The results of the female workers differed from those of the male workers at the same plant. The analyses concerning the male workers showed significantly elevated SMR values for all causes (SMR 1.12) and all cancers (SMR 1.23), but a strong healthy worker effect was observed for the female workers. The contrasting results between the male and female workers at the thorium-processing plant might be due to potentially greater thorium exposure among the male workers. Most of the male workers (78.1%) were employed as laborers and operators in the thorium extraction process, which has been known to result in high exposure to thorium (8). The majority of the females (69.6%) was, however, involved in the production of incandescent gas mantles. The exposure to thorium involved in mantle production is unknown, but was probably very low (35). If we assume that, at the beginning, the male workers had the same effect (healthy worker effect) as that of the female workers at the

plant, the real effect from thorium exposure for the male workers should be higher than the results shown in this paper.

For the male workers, the excess mortality for all cancers was statistically significant; it had been almost significant in the earlier study (SMR 1.21, 95% CI 0.99–1.48). In our current follow-up, the SMR for cancer of the pancreas was elevated, but not significantly so (SMR 1.47, 95% CI 0.70–2.71). A total of six deaths from leukemia was observed, with 5.41 deaths expected. The SMR values for cancers of the stomach, rectum, bone, prostate, lymphosarcoma, and Hodgkin's disease were all greater than one, but none of them was statistically significant. By combining mortality data on workers at the Hanford Site, Oak Ridge National Laboratory, and Rocky Flats Nuclear Weapons Plant, Gilbert et al (33) found no evidence of a correlation between radiation exposure and mortality from all cancers or from leukemia. Of the 11 other specific types of cancers analyzed, they found that multiple myeloma was the only cancer with a statistically significant correlation with radiation exposure.

In the earlier evaluation of this cohort, an excess of lung cancer was observed, although it was not statistically significant (SMR 1.44, 95% CI 0.98–2.02). In the present data the SMR for lung cancer was significantly increased (SMR 1.36, 95% CI 1.02–1.78). However, the result of the Poisson regression analysis did not show any significant effect of our study factors on mortality due to lung cancer. Smoking has been known to be a very important risk factor for lung cancer. Unfortunately, data on smoking was not available for this study. Therefore, it is difficult to conclude if there was an increased risk of lung cancer from thorium exposure in this study. Diseases of the respiratory system are of interest because of inhalation exposure at the thorium-processing plant (4). There was an increased, but not statistically significant, SMR from respiratory diseases for both the male and the female workers. Even though the observed and expected deaths from emphysema among the male workers were 13 and 7.91, respectively, there was no strong evidence for increased deaths from respiratory diseases associated with employment in this thorium-processing plant.

In summary, this study is a second follow-up of mortality among male workers and a first report of mortality among female workers at the thorium-processing plant. The SMR analyses concerning the male workers showed significantly increased mortality ratios for all causes (SMR 1.12, 95% CI 1.05–1.21), all malignant neoplasms (SMR 1.23, 95% CI 1.04–1.43), lung cancer (SMR 1.36, 95% CI 1.02–1.78), and external causes (SMR 1.37, 95% CI 1.13–1.65). On the other hand, the female workers exhibited a strong healthy worker effect, having death rates substantially below those of the general US population. A Poisson regression analysis of the data of the male workers showed

no significant effect on mortality of lung cancer from the selected factors, which included job classification, duration of employment, and time since first employment.

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