

## **Second Analysis of Mortality of Nuclear Industry Workers in Japan**

**Motoi Murata, Sumio Ohshima, Shin-ichi Kudo, Takesumi Yoshimura,  
Suminori Akiba, Toshiro Tango, Yasuhiko Yoshimoto, Yukiko Shimizu,  
Tomotaka Sobue, Shizuyo Kusumi and Hiromichi Matsudaira**

*Radiation Effects Association, 1-9-16,  
Kajicho, Chiyodaku, 101-0044 Tokyo, Japan*

### **Abstract**

A cohort study of nuclear industry workers was begun in 1990 to determine the possible health effect of low dose radiation exposure. A follow-up study of about 244,000 male workers was conducted using residence registration records. About 176,000 subjects were successfully followed up, and 5,527 deaths were ascertained during the period of observation 1986 through 1997. Underlying causes of death were identified by record linkage with magnetic tape records of national vital statistics data. The standardized mortality ratio (SMR) was calculated with Japanese males in general as the reference population. Tests for trends in death rates were made against cumulative radiation dose. The SMR (and its 95% confidence interval) was 0.90 (0.87-0.92) for all causes, 0.80 (0.77-0.84) for non-neoplastic diseases and 0.94 (0.90-0.98) for all cancer, respectively. The lower SMR was ascribed to possible healthy worker effects, etc. In the trend analyses, the death rate for neither all cancers sites nor leukemia showed any positive correlation with radiation dose, while significantly positive correlations were found for cancers of the esophagus ( $p<0.001$ ), stomach ( $p<0.05$ ) and rectum ( $p<0.05$ ), and also for external causes ( $p<0.001$ ). In lifestyle survey studies of 49,000 workers, both smoking and drinking habits were positively correlated with radiation dose. These lifestyle characteristics may have been important factors affecting the present results.

***Keywords: low level radiation, radiation effects, epidemiology, cancer***

## **Introduction**

A cohort study of nuclear industry workers was made with the aim to obtain scientific information on health effect of exposure to low-level radiation in man. This study, the conduct of which had been entrusted by the Japanese Ministry of Education, Culture, Sports, Science and Technology (MEXT), was begun in 1990 by the Institute of Radiation Epidemiology (IRE) of the Radiation Effects Association (REA) [1].

## **Materials and Methods**

### **1) Follow-up Study**

The study population consisted of approximately 244,000 radiation workers, who were registered in the Radiation Dose Registration Center (RADREC) of REA as of the end of March 1995 and who satisfied certain requirements such as having a record of exposure dose. First, personal identification information was obtained from RADREC, including central registration number, name, gender and date of birth. Next, home address information was acquired with the cooperation of nuclear facilities where the subjects worked. Then, the survival status of whether dead or alive was confirmed by obtaining residence registration certificates from the local government offices of their residence. Excluded from the analysis were workers who could not be located due to unknown address or because of expiration of the storage period (five years) for records that had been removed from the residence register due to death or relocation. The follow-up involved both retrospective and prospective observations.

For those whose death had been thus confirmed, the cause of death was ascertained by a record linkage with magnetic tape copies (1986-1997) of vital statistic death records of the Japanese Ministry of Health, Labor and Welfare. Effective dose equivalent data registered at RADREC were used as the exposure doses of the subject workers.

The "total study population" consisted of approximately 176,000 male workers identified through either the retrospective or prospective follow-up. From this population, approximately 119,000 workers, who had been prospectively followed-up, were designated as the "prospective study population". Female workers were excluded from the study populations because of the small number of cases.

### **2) Statistical Analysis**

The total period at risk was divided into three periods, 1986-1989, 1990-1994 and 1995-1997, and the range of age of the subjects 20 to 85 years was stratified into 5-year age classes. In external comparisons, the standardized mortality ratio (SMR) and its 95% confidence interval (CI) were calculated.

In internal comparisons, trend analysis with score statistics was performed. Namely, the study population was divided into five groups by cumulative dose levels of less than 10 mSv, 10-19 mSv, 20-49 mSv, 50-99 mSv and 100 mSv or more, and the statistical significance was tested for whether the ratio of observed (O) to expected (E) numbers of deaths (O/E ratio) among cumulative dose-specific groups was higher at greater cumulative doses, by adjusting for the factor of regional differences (8 major districts of Japan). The expected number of deaths in each dose group was calculated by assuming that the mortality rate was the same as the age-specific and calendar-year-specific mortality rate of the study population. Analyses were performed in two ways, either with or without consideration of the latent period to onset of cancer due to radiation (two years for leukemia and ten years for other neoplasms). Furthermore, multiple comparison analysis (Bonferroni's Method) was applied to prevent accidental judgment of "significant" during repeated multiple tests.

### 3) Lifestyle survey study

In addition to the main follow-up study, a supplementary questionnaire survey of lifestyle was conducted for about 49,000 workers to examine whether any factor with known relationship to human cancers might play a role as a confounding factor in this follow-up study.

The subjects of this survey were those actually engaged in work at nuclear facilities during the period 1997-1999, when questionnaires were distributed and collected. The questionnaire was of a self-administered type and included questions on daily habits such as tobacco smoking, alcohol intake, tea intake, etc., and also questions concerning occupational history of specific hazardous jobs and history of medical radiation exposures.

The responses were tabulated by age (<30, 30-, 40-, 50-, 60+ years) and radiation dose groups (<10, 10-, 20-, 50-, 100+ mSv). Statistical tests were carried out to examine whether the percentage of positive answers to each question showed any trend with increasing dose among the male respondents.

## Results

### 1) Characteristics of the Subject Populations

The average period at risk for the 175,939 members of the total study population was 7.9 years. The average individual cumulative dose was about 12 mSv and the total collective population dose was about 2,109 person-Sv. The mode of year of birth for the population was in the 1950s. There were 5,527 deaths, of which 2,138 were due to cancers.

The average period at risk for the 119,484 subjects in the prospective study population was about 4.5 years. The average individual cumulative dose was about 15 mSv and the total collective population dose

was about 1,826 person-Sv. The mode of year of birth for the population was in the 1950s. There were 2,934 deaths, of which 1,191 were due to cancers.

## 2) External Comparison

When the latent period was not taken into consideration, the SMR (and 95% CI) for deaths due to all causes, non-neoplastic diseases and all cancers was 0.90 (0.87-0.92), 0.80 (0.77-0.84) and 0.94 (0.90-0.98), respectively, in the total study population (Table 1), and was 0.94 (0.90-0.97), 0.86 (0.82-0.91), and 0.98 (0.93-1.04), respectively, in the prospective study population. These values are significantly less than 1 except the SMR for all cancers in the prospective study population.

On the other hand, the SMR for site-specific cancers including leukemia was not significantly different from 1 in either the total or prospective study population, irrespective of whether or not the latent period was considered. The exception is gastric cancer (SMR=0.89) in the total study population when examined without inclusion of the latent period,.

## 3) Internal Comparison

The results of internal comparisons (Table 2) presented below will focus on the prospective study population, where bias due to failure of verification of death is considered to be less probable as was seen in the results of external comparison. For neoplasms the results were limited to analyses that took the latent period into consideration. The total number of deaths due to cancer was 1,191 without consideration of the latent period, and this was reduced to 1,076 when the latent period was included.

Although the total mortality rate was increased significantly at higher cumulative doses, it was mainly ascribable to deaths due to external causes ( $p<0.001$ ). No significant trend was found for cancer in all sites ( $p=0.99$ ). Nor was it seen for leukemia ( $p=0.503$ ). The mortality rates for cancers of the esophagus ( $p<0.001$ ), stomach ( $p=0.025$ ) and rectum ( $p=0.024$ ), and for multiple myeloma ( $p=0.07$ ) showed a significant or closely significant trend related to exposure dose, and a similar trend was found in analyses that did not take the latent period into consideration. However, the trends for cancers of the stomach and rectum, and for multiple myeloma were not significant in tests by the multiple comparison method. No significant trends were found for cancers other than these sites.

## 4) Questionnaire survey study

Statistical analyses of the results of the questionnaire survey on lifestyle revealed the following characteristics for male workers at nuclear facilities in relation to the cumulative radiation dose.

- a) The percentage of tobacco smokers was significantly increased at higher doses. Furthermore, the number of cigarettes smoked per day was greater and the age of commencement of tobacco smoking was lower in

the higher dose groups.

- b) Although the percentage of alcohol drinkers did not differ among dose groups, those with higher doses tended to be heavier alcohol drinkers and younger at age when they started to drink.
- c) Regarding the habit of drinking tea and suchlike, a lower percentage of black tea drinkers was observed with increasing cumulative dose.
- d) Those in higher dose groups showed higher rates of having participated in special health examination programs and having been employed in hazardous work.
- e) Respondents in higher dose groups tended to have not received gastrointestinal X-ray examinations or other kinds of radiological examinations.

## **Discussion**

With focus on the results for the prospective study population, external comparisons showed a significantly lower total mortality rate than among average Japanese males in general, seemingly due to the healthy worker effect. The total cancer mortality rate, for which the influence of this effect is considered to be small, was nearly the same as that of the average Japanese male population. All cancers including leukemia showed no significant increase compared with the average Japanese male population.

Results of internal comparisons showed no significant trend either for cancer in all sites or for leukemia to increase with cumulative dose. Significant trends related to radiation dose were noted for some gastrointestinal tract cancers, especially esophagus cancer, but not for other cancers.

Other similar studies in various countries do not necessarily indicate a sufficiently significant association with dose for all cancers or leukemia, but for various cancers of specific sites, to make the respective conclusions incompatible [2]. These reported results, including those of the present study, are at great discrepancy, and, in many aspects, are not consistent with studies of atomic bomb survivors in Hiroshima and Nagasaki. These differences seem to be caused partly by the fact that most of the studies do not consider confounding factors such as lifestyle.

The questionnaire survey on lifestyle revealed that, in comparison with workers with lower cumulative doses, those with higher cumulative doses smoked more, drank more, worked longer hours in specific harmful operations, and participated less in gastrointestinal X-ray mass examinations. These differences in lifestyle are predicted as having confounded the results of the present study. For instance, smoking and drinking are well known to strongly influence gastrointestinal tract cancers, including esophageal cancer [3], and it is highly probable that the relationship of these cancers with cumulative dose described above had been brought about by the effect of these confounding factors.

In this context, it is very probable that certain presently unrecognized confounding factors similarly

may have had influence on external causes of death, since no biomedically plausible explanation could be given for a causative effect of radiation on such conditions.

It should also be noted that the actual period of observation in this study is still short and that the average age of the subject population was rather young.

When these points are taken into consideration, it does not seem that any conclusive evidence was obtained from the present results as to whether low-level radiation doses increase cancer mortality. To obtain more reliable scientific information on the health effects of radiation, it will be necessary to continue this kind of study over a long period, and to develop plans for the study of the effect of confounding factors.

## **References**

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**Table 1 SMRs by Cause of Death in Total Study Population (Latent Period: 0 year).**

Cause of Death	Observed Number	Expected Number	SMR	95% Confidence Interval	p Value for Two-sided Test
All Causes	5,527	6,168.8	0.90	(0.87-0.92)	0.000
All Causes (excl. unknown or external causes)	4,539	5,266.1	0.86	(0.84-0.89)	0.000
External Causes	955	902.7	1.06	(0.99-1.13)	0.085
Non-Neoplastic diseases	2,354	2,933.8	0.80	(0.77-0.84)	0.000
All Neoplastic Diseases	2,185	2,332.3	0.94	(0.90-0.98)	0.002
All Malignant Neoplasms	2,138	2,273.9	0.94	(0.90-0.98)	0.005
[By Site]					
Oral, Pharynx	38	48.3	0.79	(0.56-1.08)	0.159
Esophagus	100	119.3	0.84	(0.68-1.02)	0.085
Stomach	428	481.9	0.89	(0.81-0.98)	0.015
Colon	144	141.6	1.02	(0.86-1.20)	0.875
Rectum	95	109.5	0.87	(0.70-1.06)	0.180
Liver	405	390.2	1.04	(0.94-1.14)	0.471
Gallbladder	70	73.1	0.96	(0.75-1.21)	0.765
Pancreas	127	129.5	0.98	(0.82-1.17)	0.860
Lung	397	410.9	0.97	(0.87-1.07)	0.510
Prostate	32	33.8	0.95	(0.65-1.34)	0.818
Bladder	27	23.4	1.15	(0.76-1.68)	0.525
Kidney and Other and Unspecified Urinary Organs	32	37.4	0.86	(0.58-1.21)	0.421
Brain and Central Nervous System <sup>(a)</sup>	26	37.7	0.69	(0.45-1.01)	0.067
Leukemia <sup>(b)</sup>	60	67.6	0.89	(0.68-1.14)	0.390
Non-Hodgkin's lymphoma	46	57.3	0.80	(0.59-1.07)	0.153
Multiple Myeloma	20	17.8	1.12	(0.69-1.74)	0.685
All Malignant Neoplasm except Leukemia	2,078	2,206.3	0.94	(0.90-0.98)	0.007

(a) Neoplasm of malignant, benign and unspecified.

(b) Number of cases for chronic lymphatic leukemia was zero.

**Table 2 Trend Analysis by Cause of Death in Prospective Study Population with Latent Periods for Cancers.**

Cause of Death	Cumulative Dose Group (mSv)					p-Value for One-sided Trend
	<10	10~	20~	50~	100+	
All Causes	2014 <sup>(a)</sup> 2085.7	320 291.5	349 310.1	138 152.4	113 94.2	0.017
All Causes (excl.unknown or external causes)	1767 1805.4	269 247.0	292 261.8	107 127.2	85 78.5	0.296
External Causes	236 268.6	46 42.7	56 46.4	31 24.2	28 15.1	0.000
Non-Neoplastic diseases	914 936.6	142 128.0	150 135.1	57 65.1	42 40.2	0.371
All Neoplastic diseases	785 810.1	118 107.5	126 110.6	42 47.9	25 19.9	0.119
All Malig.Neopl.	770 795.1	115 105.4	124 108.7	42 47.2	25 19.6	0.099
[By Site]						
Oral, Pharynx	17 16.1	2 2.2	3 2.2	0 1.0	0 0.5	0.840
Esophagus	28 37.5	6 4.7	5 4.7	8 2.1	3 0.9	0.000
Stomach	136 153.2	28 20.6	26 21.2	13 9.2	5 3.8	0.025
Colon	47 45.8	3 5.4	7 5.5	2 2.3	1 0.9	0.507
Rectum	29 32.8	3 4.4	7 4.7	4 2.1	2 1.0	0.024
Liver	149 152.5	21 21.0	25 21.0	6 9.0	6 3.5	0.205
Gallbladder	38 32.1	3 4.3	2 4.7	0 2.0	1 1.0	0.917
Pancreas	44 44.0	8 6.0	6 6.3	1 2.7	1 1.0	0.723
Lung	161 161.4	25 20.7	25 21.7	3 9.3	3 4.0	0.884
Prostate	18 15.9	0 1.9	0 1.9	2 0.9	1 0.4	0.229
Bladder	12 9.1	0 1.4	1 1.6	0 0.7	0 0.3	0.909
Kidney & Other Urinary	11 13.8	4 2.0	4 2.0	0 0.9	0 0.4	0.600
Brain & C.N. System <sup>(b)</sup>	7 5.7	1 0.9	0 0.9	0 0.4	0 0.1	0.856
Leukemia <sup>(c)</sup>	19 19.3	2 2.8	5 3.2	1 1.7	1 1.0	0.503
Non-Hodgkin's Lymphoma	13 13.3	1 1.7	3 1.8	1 0.8	0 0.3	0.523
Multiple Myeloma	5 4.6	0 0.6	0 0.6	0 0.2	1 0.1	0.070
All Malig. Neopl. Except Leukemia	754 777.7	112 103.0	121 106.1	41 46.0	24 19.1	0.116

(a) Observed and expected numbers of deaths in the upper and lower parts, respectively.

(b) Malignant, benign and unspecified neoplasms were included.

(c) Number of cases for chronic lymphatic leukemia was zero.