e-cell gel ele
al. on p. 67

Paper

# MORTALITY OF WORKERS AT THE HANFORD SITE: 1945–1986

Ethel S. Gilbert,* Ellen Omohundro,† Jeffrey A. Buchanan,* and Nancy A. Holter*

*Abstract*—Updated analyses of mortality of workers at the Hanford site provide little evidence of a positive correlation of cumulative occupational radiation dose and mortality from leukemia and from all cancer except leukemia. Estimates of the excess relative risk per 10 mSv were negative for both disease categories, but these estimates are consistent both with no risk and with estimates obtained through extrapolation from high-dose data. For all cancer except leukemia, the upper limit for a two-sided 90% confidence interval was about 1.5 times the prediction of the BEIR V model, but several times the estimate recommended by the ICRP 60 committee. For leukemia, the comparable upper limit was very close to that predicted by either BEIR V or ICRP 60. The all-cancer risk estimate, from a recent report on updated analyses of data for Oak Ridge National Laboratory workers, was strongly rejected based on the Hanford data. Of 24 specific cancer categories evaluated, only cancer of the pancreas and Hodgkin's disease showed positive correlations with radiation dose that approached statistical significance with one-tailed $p$ values of 0.07 and 0.04, respectively; these correlations are interpreted as probably spurious. For multiple myeloma, for which a correlation was reported previously, the $p$ value was 1.10. However, a significant correlation ($p < .05$) was obtained when analyses were expanded to include deaths with multiple myeloma listed on the death certificate but not considered to be the underlying cause, when analyses were expanded to include deaths occumng in Washington State during the time period 1987–1989, or when a 2-y latency period (instead of 10-y) was assumed.

Health Phys. 64(6):577–590; 1993

Key words: mortality; cancer, radiation dose; risk estimates

## INTRODUCTION

RESULTS of several studies of nuclear workers have been reported (Beral et al. 1985, 1988; Smith and Douglas 1986: Wing et al. 1991; Kendall et al. 1992), and for the most part have indicated effects that are consistent with risk estimates that have been obtained through extrapolation from high-dose data. Recently, however, an estimate based on updated data (through 1984) on Oak Ridge National Laboratory (ORNL) workers was found to be about 10 times the estimate obtained through linear extrapolation from Japanese atomic bomb (A-bomb) survivor data (Wing et al. 1991). Because this finding was different from the result based on earlier data, and because the effect was strongest when a minimal latent period of 20 y was assumed, Wing et al. (1991) suggested that the longer follow-up period for this cohort might account for the seeming discrepancy between the ORNL findings and those from several other worker studies.

Results of analyses of mortality of Hanford workers for the time period 1945–1981 were reported by Gilbert et al. (1989a) and provided little evidence of a correlation of radiation dose and overall cancer mortality. The purpose of this paper is to update these analyses to include an additional 5 y (1982–1986) and, particularly, to investigate whether the longer follow-up period might modify results in a manner similar to that observed in ORNL workers. An additional objective is to provide a more rigorous comparison with estimates obtained through extrapolation from high-dose data; at the time the 1989 paper was prepared, risk estimates based on revised Japanese A-bomb dosimetry were not available, and the report of the BEIR V committee (National Academy of Science 1990) and recommendations of the International Commission on Radiation Protection (1991) had not been published. The earlier paper also included supplementary analyses including deaths occumng in the state of Washington for 1982–1985. In this paper, similar supplementary analyses include Washington deaths for 1987–1989.

## THE STUDY POPULATION

The study population, the radiation exposure data, and the methods used to determine vital status and cause of death, were described by Gilbert et al. (1989a), which is referred to hereafter as the "1989 paper" or as "1989 analyses." These elements are described only briefly here, with emphasis on modifications that have been made.

As in the 1989 analyses, the study population consisted of all workers, other than those employed only in construction activities, initially employed at the Hanford site from 1944–1978 by U.S. Department of Energy contractors. Whether a worker was a member

* Pacific Northwest Laboratory, P.O. Box 999, Richland, WA 99352; † Hanford Environmental Health Foundation, P.O. Box 100, Richland, WA 99352.

(*Manuscript received* 30 *June* 1992; *revised manuscript received* 4 *December* 1992, *accepted* 15 *January* 1993)
0017-9078/93/$3.00/0

of the study population was determined through the use of employment histories, which have been maintained by the Hanford Environmental Health Foundation since the mid-1960s when the study was initiated. Since the 1989 publication, extensive efforts have been made to refine the database used for statistical analyses, and these efforts are described in detail by Gilbert et al. (1992). Here it is noted only that these efforts resulted in the removal of 265 workers primarily because current records indicate they did not actually start employment at Hanford (they had appeared in the employment histories because they had participated in preemployment physical examinations), and the addition of 456 workers who did not have employment history records at the time our earlier data base was prepared. Some corrections to dosimetry and employment data used in previous analyses were also made. To investigate the possible effects of these modifications, the main analysis presented in Table 3 of the 1989 paper was redone, using identical methodology but with the modified data. The results differed very little from the published results based on old data.

Two Hanford workers who were involved in incidents in which more than 250 mSv was received on a single occasion were also excluded from the study population used in analyses in this paper; these workers died of circulatory diseases in 1987 and 1988, respectively. Unlike analyses in the 1989 paper, internal comparisons by dose in this paper were restricted to workers employed at Hanford for at least 6 mo. This restriction was made for comparability with past and future analyses of combined mortality data on workers at Hanford, Oak Ridge National Laboratory, and Rocky Flats Weapons Plant (Gilbert et al. 1989b), where it was judged more appropriate to exclude extremely short-term workers.

## Vital status

Vital status was established by periodic searches of earnings and benefits files of the Social Security Administration **(SSA)** (1944–1986), by the use of the U.S. National Death Index (NDI) (1979–1986), and through linkages (of Social Security numbers and names) with the State of Washington vital statistics computerized files for 1968–1989 and the State of California vital statistics computerized files for 1960–1986. In our 1989 paper, we determined that the proportion of deaths in the State of Washington (where mortality ascertainment should be close to 100% complete), also identified through the **SSA** or NDI, was 97%. A study to gain better information on the adequacy of follow-up is currently underway. For now, we note that the internally based comparisons emphasized in this paper are less likely to be biased because of inadequate follow-up than comparisons of death rates with those of the general population. The National Center for Health Statistics codes all medical conditions recorded on death certificates and also assigns the underlying cause of death.

## External radiation exposure data

External dose estimates are expressed in millisievert (mSv). Because exposures were primarily to low linear-energy-transfer gamma radiation, the absorbed dose (mGy) and dose equivalent (mSv) were similar for most workers. Thus, we refer to "dose" even though "dose equivalent" is more accurate terminology. Although some members of the study population also performed construction work either prior or subsequent to their employment in operations work, data on these doses had not been extracted for files used to perform 1989 analyses of the Hanford data; thus, the 1989 analyses were based only on dose received in operations work. In this paper, dose incurred while performing such construction work was included but, for comparison with previous results, supplementary analyses were performed with this dose excluded.

Table 1 shows the number of subjects in the study population by gender, by whether or not they were monitored for external radiation, and by whether or not they were employed at the Hanford site for at least 6 mo. It also shows the total person-Sv and the average dose accumulated through 1985 by monitored workers. Of the 861 person-Sv recorded for the total population, 26 person-Sv were received in construction work. About 99% of the total dose was received by workers

**Table 1.** Number of workers, number of monitored workers, total dose, and average cumulative dose through 1985 by gender and length of employment.

| | Number of workers | Number of monitored workers | Total person-Sv | Average cumulative dose[a] (mSv) |
|---|---|---|---|---|
| All workers | 44,154 | 36,971 | 861.0 | 23.3 |
| Male | 31,486 | 28,086 | 814.5 | 29.0 |
| Female | 12,668 | 8,885 | 46.5 | 5.2 |
| Employed 6+ mo | 36,439 | 32,643 | 854.1 | 26.2 |
| Male | 25,998 | 24,672 | 808.1 | 32.8 |
| Female | 10,441 | 7,971 | 46.0 | 5.8 |
| Employed <6 mo | 7,715 | 4,328 | 6.9 | 1.6 |
| Male | 5,488 | 3,414 | 6.4 | 1.9 |
| Female | 2,227 | 914 | 0.5 | 0.5 |

[a] Based on workers monitored for external radiation.

employed at least 6 mo, and 95% was received by male workers. The additional 5y of follow-up increased the total person-year-Sv (calculated with a 10-y lag) by about 50% (from 5,300 to 8,000).

### Socioeconomic status

Analyses in this paper were based primarily on internal comparisons by level of radiation exposure. A possible source of bias in these comparisons is that those workers performing jobs involving radiation exposure may have different socioeconomic characteristics than workers performing otherjobs. For this reason, previous analyses of the Hanford data have made use of a general occupational category determined from Bureau of Census codes (1971), and some studies of nuclear workers in the UK have adjusted analyses for social class (Beral et al. 1985, 1988).

Since our 1989 paper, job category data for Hanford workers have been used to define a socioeconomic variable that is similar to the social class variable used in the UK studies, which was also based on job category data. We make use of four general socioeconomic categories, as defined in Table 2. Workers were assigned to the general category in which they had spent the longest period of time from initiation of Hanford employment through the end of 1985. About 72% of the study population spent their entire employment period at Hanford in a single general category, while 88% spent at least 75% of their employment period in a single category. From Table 2, it can be seen that about 77% of the total person-Sv was received by workers assigned to the skilled and semiskilled manual category, while only about 3.5% was received by workers assigned to the clerical and unskilled categories. All four categories included substantial numbers of workers with very little occupational dose; the proportions of workers who had accumulated total doses <10 mSv were 65%, 70%, 47%, and 84% for the four respective categories shown in Table 2.

## STATISTICAL METHODS

The methods used to analyze these data have been described elsewhere (Gilbert and Buchanan 1984; Gilbert 1989; Gilbert et al. 1989a and b); a nontechnical discussion of methods for analyzing data from studies of nuclear workers is given by Gilbert (1991). Here, we provide only sufficient detail to indicate the specific approach used in this paper.

External comparisons were made by calculating standardized mortality ratios **(SMRs)** based on age-gender-calendar year-specific death rates for the **U.S.** using software developed by Monson (1974), which currently includes **U.S.** death rates through 1985. However, because good dose measurements were available, and because dose varied considerably among workers, as in previous analyses, we emphasize analyses based on internal comparisons of death rates by level of radiation dose. Such comparisons are less subject to bias, and more likely to detect risks resulting from radiation exposure than are external comparisons.

The trend test statistic used to evaluate the association of cumulative radiation dose with death from several causes is sensitive to an increase in death rates with increasing exposure. The trend test was based on individual dose values rather than scores for dose categories. In addition, observed and expected deaths were calculated for five dose categories using the Mantel-Haenszel method (Mantel and Haenszel 1958). These calculations were made using the computer software MOX (Gilbert and Buchanan 1984). In all cases in which the test statistic exceeded 1.645, the one-tailed p value was estimated using computer simulations based on 10,000 samples, as described in Gilbert (1989). Because of the highly skewed exposure distribution, this procedure provides a more accurate assessment than would the usual asymptotic normal approximation. These simulations were based on eleven dose categories (0–, 5–, 10–, 20–, 50–, 100–, 150–, 200–, 300–, 400–, and 500+ mSv) rather than on the individual dose

Table 2. Number of workers, total dose, and average cumulative dose through 1985 among monitored workers employed at least 6 mo at the Hanford site by longest general socioeconomic category.

| General socioeconomic category | Corresponding social class[a] | Number of workers | Total person-Sv | Average cumulative dose (mSv) |
|---|---|---|---|---|
| Professional and technical[b] | I and II | 14,028 | 248.2 | 17.7 |
| Clerical[c] | IIINM | 6,487 | 23.4 | 3.6 |
| Skilled and semiskilled manual[d] | IIIM and IV | 10,875 | 576.0 | 53.0 |
| Unskilled manual[e] | V | 1,253 | 6.5 | 5.2 |

[a] These are the corresponding social classes used in the UK.
[b] Professional, technical, and managerial workers with Bureau of Census Codes 001–245, and 265.
[c] NM = nonmanual. Clerical workers with Bureau of Census Codes 280, and 301–395.
[d] M = manual. Skilled and semiskilled manual workers with Bureau of Census Codes 401–575, 590,600–726, 755, 912–916, and 961–995. The Bureau of Census codes were expanded for use with the Hanford study. Special codes developed were 590 for supervisory manual workers, 691 for radiation monitors, 692 for process operators, 693 for reactor operators, 694 for utility operators (unspecified as to type), 695 for power operators, and 696 for other operators.
[e] Unskilled workers with Bureau of Census Codes 740–954. except 912–916.

values. Latency time periods were allowed for by conducting analyses based on cumulative dose calculated with 2–, 10–, and 20-y lags.

For all analyses, stratification variables included gender, age (25–29, 30–34, single-year intervals for ages 35–80, 80–84, and 85+), and calendar year (1945–1949, 1950–1954, 1955–1959, 1960–1964, 1965–1969, 1970–1974, 1975–1979, 1980–1981, 1982–1984, and 1985–1986). Unless stated otherwise, analyses also included stratification on number of years monitored (1–4, 5+) and on the four socioeconomic categories shown in Table 2. Number of years monitored was selected because of a demonstrated effect of this variable in past analyses of the Hanford data (Gilbert 1989), and for consistency with previous analyses. Analyses of the newly defined socioeconomic categories indicate that this variable is an important predictor of risk.

For example, relative risks (with 90% confidence intervals) for all cancer, expressed relative to the professional and technical category, were 1.1 (0.9, 1.3) for clerical workers, 1.3 (1.1, 1.4) for skilled and semiskilled workers, and 1.5 (1.2, 1.8) for unskilled workers. These results, along with the association with radiation dose shown in Table 2, indicate that socioeconomic status is a potentially important confounder.

Workers were entered into the analysis at the beginning of the year following the initial employment year plus five, or the first year of monitoring, whichever occurred later. For example, a worker who initiated employment in 1950, and received doses of 10 mSv, 5 mSv, and 25 mSv in 1950, 1951, and 1952, respectively, would begin contributing person-years at the beginning of 1956. With a 10-y lag, this worker would be assigned 0 mSv for each of the years 1956–1960, 10 mSv for the year 1961, 15 mSv for the year 1962, and 40 mSv for 1963 and all succeeding years of follow-up.

The first 5 y of follow-up were excluded to allow for the possibility of an especially strong healthy worker effect present during this time period, and because cancers occurring during this period are highly unlikely to be the result of occupational exposure. It is noted that when doses are lagged for 5 or more years (as in most analyses in this paper), excluding the first 5 y is equivalent to stratification on follow-up period with two strata, <5 y and ≥5 y; this is true because all workers have zero dose for the first 5 y of follow-up and, thus, there is no information available for internally based comparisons. With the shorter 2-y lag period, leukemia is the disease of primary interest; there were three leukemia deaths during the first 5 y of follow-up, but none had doses exceeding 5 mSv.

The choices just given are those that are emphasized on an *a priori* basis, but analyses based on several alternative choices are also presented. For leukemia, we emphasize analyses based on the 2-y lag period, while for other cancers, we emphasize the 10-y lag period; these are the choices used in most radiation risk assessment efforts.

Estimates and confidence limits for cancer risks per unit of dose were calculated based on a model in which the relative risk was assumed to be of the form $1 + \beta Z$, where Z is the cumulative dose, and $\beta$ is expressed as a percent increase per 10 mSv. These estimates were obtained by maximizing the likelihood function with confidence limits obtained by use of the score statistic (Gilbert 1989). The score statistic is easier to apply if based on grouped rather than individual dose measurements; for this purpose, we used the 11 dose categories previously indicated. For leukemia, a simulation procedure was used to determine confidence limits as described in Gilbert (1989). Ninety percent confidence intervals are emphasized, but some results are presented with both 90 and 95% confidence intervals.

## RESULTS

### Comparison with U.S. rates

In Tables 3 and 4, SMRs are presented for monitored and unmonitored male and female workers. Workers employed <6 mo were included in these calculations. The all-cause SMR was 0.82, compared with 0.79 reported in 1989. The SMR for all malignant neoplasms was 0.86, compared with 0.85 reported in 1989.

The SMRs for diseases of the musculoskeletal system, for cancer of the pancreas in unmonitored males and for all other solid tumors in unmonitored males were elevated based on earlier data and remained so in these updated analyses. The previously elevated SMR for lung cancer in females was no longer elevated. The results in Tables 3 and 4 generally show a strong healthy worker effect. The highest SMR for specific cancers in all workers was 1.03 for the "all other solid tumors" category.

### Radiation exposure analyses

Table 5 shows detailed results of analyses that examine the trend in death rates from many diseases with increasing exposure. Table 6 shows relative risks by dose category for cancers, noncancers, leukemia, and multiple myeloma. For noncancers, the direction of the correlation of radiation exposure and mortality was negative with a stronger correlation for the 2-y lag than for the 10-y lag. Deaths from accidents, poisonings, and violence showed a particularly strong negative correlation. The categories of respiratory diseases (excluding pneumonia) and cirrhosis were examined to provide insights regarding possible differential smoking and drinking habits by exposure category. Neither of these disease categories was strongly correlated with radiation dose.

The direction of the correlations for both all-cancers and leukemia was negative whether analyses were based on 2-y or 10-y lags. In 1989 analyses, the correlation for all cancers in females was positive and approached statistical significance, but this correlation was no longer close to statistical significance. Results

Table 3. Standardized mortality ratios[a] (SMRs) and observed deaths (OBS) for major causes of death in monitored and unmonitored white male and female Hanford Site workers from 1945–1986.

| Cause of death (eighth revision ICD[b] code) | Males | | | | Females | | | | All workers | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Monitored | | Unmonitored | | Monitored | | Unmonitored | | | |
| | SMR | OBS | SMR | OBS | SMR | OBS | SMR | OBS | SMR | OBS |
| All causes of death | 0.81 | 6,678 | 0.90 | 1,441 | 0.76 | 713 | 0.82 | 620 | 0.82 | 9,452 |
| Infective and parasitic disease (000–136) | 0.28 | 30 | 0.25 | 6 | 0.27 | 3 | 0.39 | 4 | 0.28 | 43 |
| Malignant neoplasms (140–209) | 0.86 | 1,508 | 0.90 | 280 | 0.81 | 224 | 0.87 | 183 | 0.86 | 2,195 |
| Benign and unspecified neoplasms (210–239) | 0.54 | 12 | 0.74 | 3 | 0.00 | 0 | 1.35 | 5 | 0.58 | 20 |
| Endocrine, metabolic, and nutritional diseases (240–279)' | 0.91 | 126 | 0.94 | 24 | 0.64 | 17 | 0.67 | 14 | 0.86 | 181 |
| Diseases of blood and blood-forming organs (280–289) | 0.42 | 8 | 0.99 | 4 | 0.94 | 3 | 0.76 | 2 | 0.59 | 17 |
| Mental disorders (290–315)' | 0.71 | 33 | 1.21 | 9 | 0.89 | 4 | 1.47 | 5 | 0.82 | 51 |
| Diseases of the nervous system and sense organs (320–389) | 0.86 | 67 | 0.50 | 7 | 1.02 | 13 | 0.73 | 7 | 0.82 | 94 |
| Diseases of the circulatory system (390-458) | 0.82 | 3,377 | 0.87 | 729 | 0.65 | 244 | 0.70 | 223 | 0.81 | 4,573 |
| Diseases of the respiratory system (460–519) | 0.86 | 449 | 1.01 | 106 | 1.03 | 47 | 1.16 | 42 | 0.91 | 644 |
| Diseases of the digestive system (520–577) | 0.67 | 250 | 1.06 | 70 | 1.03 | 43 | 1.06 | 35 | 0.78 | 398 |
| Diseases of genito-urinary system (580–629) | 0.57 | 64 | 0.84 | 22 | 0.21 | 3 | 0.64 | 8 | 0.59 | 97 |
| Diseases of skin and subcutaneous tissue (680–709) | 0.16 | 1 | 0.79 | 1 | 0.00 | 0 | 2.41 | 3 | 0.49 | 5 |
| Diseases of the musculoskeletal system and connective tissue (710–738) | 1.30 | 18 | 1.21 | 3 | 2.06' | 9 | 0.94 | 3 | 1.38' | 33 |
| Symptoms and illdefined conditions (780–796) | 0.51 | 45 | 0.99 | 15 | 0.63 | 6 | 0.29 | 2 | OS7 | 68 |
| Accidents, poisonings, and violence (800–999) | 0.82 | 591 | 1.09 | 125 | 1.09 | 69 | 1.35 | 58 | 0.90 | 843 |
| Cause unavailable | | 85 | | 34 | | 22 | | 26 | | 167 |

[a] The SMR is the ratio of observed to expected deaths, where expected deaths are calculated from age-specific and calendar year-specific mortality rates for U.S. white males or females. The SMRs are corrected for those deaths with no certificates on the assumption that the distribution of causes is similar for those with and without certificates.
[b] ICD = International Classification of Diseases, Eighth Revision.
'These SMRs are based on the years 1950–1986 since U.S. mortality rates for these categories were not available prior to 1950. For this reason, and because separate calculations for ICD codes 740–759 (congenital malformations) are not included in the Monson software, the sum of deaths from specific causes is less than the total.
[d] Significantly elevated at the 0.05 level based on a one-tailed test.

of separate analyses for cancers that have been linked with smoking (Doll and Peto 1981) and those that have not been so linked were similar; although, the correlation for the smoking-related cancers was more positive than for the remainder.

Twenty-four separate cancer categories were analyzed. For both the 10- and 2-y lags, the numbers of positive and negative trend test statistic were approximately equal. It is evident that with 24 categories and 2-y lag periods, some categories are likely to demonstrate individual one-tailed $p$ values of $<0.05$ by chance alone.

Multiple myeloma, which has previously been the cancer type most strongly linked with radiation dose in the Hanford data, did not exhibit a statistically significant correlation with the 10-y lag ($p = .10$), but did demonstrate such a correlation with the 2-y lag ($p = .008$). In 1989 analyses, the category of other female genital cancers (the combined categories of cancer of the cervix, uterus, and ovary) demonstrated a correlation of borderline statistical significance. With the updated data, the trend test statistics for this combined category were 1.13 for a 10-y lag and 0.66 for a 2-y lag, neither close to statistical significance.

Table 5 shows a statistically significant correlation for Hodgkin's disease with both 10- and 2-y lags, and cancer of the pancreas shows such a correlation with the 2-y lag. Neither disease showed a statistically significant correlation in 1989 analyses, but cancer of the pancreas exhibited a statistically significant correlation in much earlier analyses (Gilbert and Marks 1979). Cancer of the liver shows a correlation of borderline statistical significance with a 2-y lag, but not with a 10-y lag.

Table 4. Standardized mortality ratios[a] (SMRs) and observed deaths (OBS) for specific cancer types in monitored and unmonitored white male and female Hanford Site workers from 1945–1986.

| Type of cancer (eighth revision ICD[b] code) | Males | | | | Females | | | | All workers | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Monitored | | Unmonitored | | Monitored | | Unmonitored | | | |
| | SMR | OBS | SMR | OBS | SMR | OBS | SMR | OBS | SMR | OBS |
| Buccal cavity and pharynx (140–149) | 0.81 | 42 | 0.66 | 6 | 0.00 | 0 | 1.08 | 3 | 0.76 | 51 |
| Digestive organs and peritoneum (150–159) | 0.87 | 414 | 0.80 | 72 | 0.74 | 46 | 0.75 | 37 | 0.84 | 569 |
| Esophagus (150) | 0.84 | 35 | 0.56 | 4 | 0.00 | 0 | 1.75 | 3 | 0.80 | 42 |
| Stomach (151) | 0.84 | 70 | 0.46 | 8 | 0.82 | 6 | 0.66 | 4 | 0.77 | 88 |
| Colon (153) | 0.88 | 141 | 0.71 | 21 | 0.70 | 19 | 0.84 | 18 | 0.84 | 199 |
| Rectum (154) | 0.72 | 35 | 0.41 | 4 | 0.52 | 3 | 0.85 | 4 | 0.67 | 46 |
| Liver and gall bladder (155–156) | 1.01 | 37 | 0.86 | 6 | 0.85 | 5 | 0.64 | 3 | 0.94 | 51 |
| Pancreas (157) | 0.91 | 84 | 1.57[d] | 26 | 0.85 | 10 | 0.56 | 5 | 0.96 | 125 |
| Respiratory system (160–163) | 0.80 | 491 | 0.93 | 93 | 1.02 | 41 | 0.97 | 28 | 0.83 | 653 |
| Larynx (161) | 0.60 | 15 | 1.36 | 6 | 1.19 | 1 | 1.61 | 1 | 0.74 | 23 |
| Lung (162) | 0.80 | 470 | 0.92 | 87 | 1.01 | 39 | 0.97 | 27 | 0.84 | 623 |
| Bone (170) | 0.44 | 3 | 0.74 | 1 | 1.13 | 1 | 0.00 | 0 | 0.51 | 5 |
| Skin (172–173) | 0.76 | 25 | 0.97 | 5 | 0.94 | 4 | 0.66 | 2 | 0.80 | 36 |
| Female breast (174) | | | | | 0.95 | 60 | 0.89 | 42 | 0.92 | 102 |
| All uterus (180–182) | | | | | 0.33 | 7 | 0.99 | 17 | 0.63 | 24 |
| Other female genital organs (183–184) | | | | | 0.78 | 16 | 1.02 | 16 | 0.89 | 32 |
| Prostate (185) | 0.95 | 116 | 1.00 | 27 | | | | | 0.96 | 143 |
| Testes and other male genital organs (186–187) | 0.71 | 6 | 1.44 | 2 | | | | | 0.82 | 8 |
| Bladder (188) | 0.68 | 34 | 0.67 | 7 | 0.36 | 1 | 1.34 | 3 | 0.69 | 45 |
| Kidney (189) | 0.94 | 41 | 1.22 | 9 | 0.72 | 3 | 0.63 | 2 | 0.95 | 55 |
| Eye (190)[c] | 1.43 | 2 | 0.00 | 0 | 0.00 | 0 | 0.00 | 0 | 0.97 | 2 |
| Brain and other central nervous system (191–192) | 0.96 | 48 | 0.52 | 4 | 0.78 | 6 | 0.53 | 3 | 0.86 | 61 |
| Thyroid (193)[c] | 0.61 | 2 | 1.74 | 1 | 1.19 | 1 | 0.00 | 0 | 0.75 | 4 |
| All other solid tumors (171, 194–199) | 1.02 | 126 | 1.47[d] | 31 | 0.81 | 16 | 0.80 | 12 | 1.03 | 185 |
| All lymphatic and haematopoietic cancer (200–209) | 0.96 | 158 | 0.76 | 22 | 0.92 | 22 | 1.01 | 18 | 0.93 | 220 |
| Lymphosarcoma and reticulosarcoma (200)[c] | 1.04 | 32 | 0.37 | 2 | 0.92 | 4 | 1.48 | 5 | 0.98 | 43 |
| Hodgkin's disease (201) | 0.93 | 16 | 1.03 | 3 | 1.26 | 3 | 0.56 | 1 | 0.94 | 23 |
| Multiple myeloma (203) | 0.93 | 21 | 1.29 | 5 | 0.83 | 4 | 0.55 | 2 | 0.91 | 32 |
| Leukemia and aleukemia (204–207) | 0.84 | 56 | 0.74 | 9 | 0.76 | 7 | 1.16 | 8 | 0.84 | 80 |
| Other lymphatic tissue (202–203,208–209)[c] | 0.99 | 50 | 0.98 | 8 | 1.02 | 8 | 0.70 | 4 | 0.97 | 70 |

[a] The SMR is the ratio of observed and expected deaths, where expected deaths were calculated from age-specific and calendar year-specific mortality rates for U.S. Caucasian males or females. The SMRs were corrected for those deaths with no certificates on the assumption that the distribution of causes was similar for those with and without certificates.
[b] ICD = International Classification of Diseases, Eighth Revision.
[c] These SMRs are based on the years 1950–1986 since U.S. mortality rates for these cancer types were not available prior to 1950.
[d] Significantly elevated at the 0.05 level based on a one-tailed test.

Table 7 shows excess relative risk estimates based on several categories of cancer, including the broad categories chosen for risk modeling by the BEIR V Committee (National Academy of Science 1990). Most estimates were very close to zero and, in all cases, confidence limits included zero risk. Confidence limits were especially wide for cancer in females because of the smaller number of females and the limited dose received by females (see Table 1). The upper confidence limits based on analyses of cancer linked with smoking were very close to those based on all cancers; analyses of cancers not linked with smoking are possibly less subject to bias than analyses of all cancers.

Analyses comparing death rates in workers with two levels of confirmed plutonium depositions (<74 74+ Bq) to those of other workers without such depositions were also performed. Both the approach and the results of these analyses were similar to those reported in the 1989 paper, with no evidence of a positive correlation of plutonium depositions with cancer death rates. The relative risks (with 90% confidence limits) for all cancers of those with <74 Bq and those with 74+ Bq relative to workers with no plutonium depositions were 0.7 (0.4, 1.2) and 0.9 (0.5, 1.6), respectively.

## Alternative radiation exposure analyses

Certain choices in the manner that dose-response analyses are conducted are necessarily arbitrary

Table 5. Results of analyses of external dose in monitored workers employed at the Hanford Site for at least 6 mo. Except where noted, this is based on a 10-y lag.

| Cause of death | Trend test statistic[a] Exposure lagged for: 10 y | 2 y | Observed and expected deaths by exposure category (mSv) e Obs/Exp[b] | 10– Obs/Exp | 50– Obs/Exp | 100– Obs/Exp | 200+ Obs/Exp |
|---|---|---|---|---|---|---|---|
| All causes | –0.90 | –1.91 | 4,341/4,267.7 | 1,333/1,378.9 | 2 131227.9 | 158/ 169.8 | 1551155.7 |
| Cause unavailable | –1.28 | –1.32 | 61/59.0 | 22119.5 | 0/3.2 | 2/2.1 | 1/2.1 |
| All cancer | –0.29 | –0.50 | 975/982.9 | 3461334.6 | 58160.1 | 47144.9 | 40143.5 |
| Male | –0.29 | –0.54 | 8161818.8 | 3161310.7 | 55156.4 | 43141.5 | 40/42.7 |
| Female | 0.02 | 0.28 | 159/ 164.2 | 30123.9 | 3/3.7 | 4/3.4 | 0/0.8 |
| Smoking-linked cancers[c] | 0.10 | -0.0 I | 380/389.0 | 154/ 148.3 | 30126.9 | 22120.7 | 19/20.I |
| Residual | –0.49 | –0.67 | 5951593.9 | 192/186.3 | 28133.2 | 25124.2 | 21123.4 |
| Buccal | –1.45 | –1.58 | 24/22.3 | 8/7.3 | 0/1.3 | 1/1.0 | 0/1.1 |
| Esophagus | 0.14 | –0.38 | 20118.6 | 5/5.9 | 1/1.1 | 0/0.7 | 1/0.7 |
| Stomach | 0.18 | 0.37 | 43144.1 | 14/12.7 | 2/2.5 | 3/1.9 | 1/1.9 |
| Colon | –0.35 | –0.63 | 103/ 106.6 | 36129.1 | 2/4.7 | 4/3.1 | 2/3.4 |
| Rectum | 0.40 | 0.14 | 25/22.9 | 6/7.7 | 1/1.4 | 1/0.9 | 1/1.0 |
| Liver | 1.37 | 1.93' | 15/14.5 | 3/3.9 | 0/0.6 | 0/0.6 | 2/0.4 |
| Gallbladder | –1.27 | –1.30 | 13110.8 | 1/2.5 | 0/0.3 | 0/0.3 | 010.06 |
| Pancreas | 1.59[d] | 2.36[d] | 51/52.5 | 19118.3 | 2/3.I | 3/2.2 | 3/1.9 |
| Larynx | –0.62 | –0.94 | 9/8.5 | 3/3.0 | 1/0.6 | 0/0.5 | 0/0.3 |
| Lung | 0.16 | 0.01 | 256/265.0 | 107/ 104.2 | 24/ 19.2 | 17/15.0 | 14/ 14.6 |
| Bone | –0.68 | –0.70 | 3/2.3 | 0/0.4 | 0/0.1 | 010.1 | 010.03 |
| Female breast | –0.05 | 0.58 | 45/46.5 | 7/5.3 | 1/0.9 | 1/1.0 | 0/0.3 |
| Cervix and uterus | 0.96 | 0.29 | 3/5.0 | 3/0.8 | 010.2 | 010.06 | 0/0.00 |
| Ovary | 0.79 | 0.61 | 12112.1 | 1/1.5 | 010.2 | 110.2 | 010.04 |
| Prostate | –1.15 | –1.51 | 59161.7 | 32127.1 | 5/4.4 | 2/3.4 | 2/3.4 |
| Bladder | –0.34 | –0.66 | 17118.9 | 11/8.7 | 1/1.3 | 1/1.0 | 1/1.1 |
| Kidney | 0.72 | 0.60 | 27123.3 | 2/7.9 | 2/1.4 | 3/1.2 | 1/1.2 |
| Brain and central nervous system | –0.90 | –0.66 | 28130.1 | 16/1 1.3 | 1/2.4 | 2/1.7 | 0/1.5 |
| Thyroid | –0.42 | –0.46 | 2/1.7 | 111.0 | 010.2 | 0/0.1 | 0/0.0 |
| Non-Hodgkin's lymphoma | –0.85 | –1.14 | 37139.1 | 17/13.7 | 3/2.6 | 1/1.8 | 1/1.8 |
| Hodgkin's disease | 1.80' | 2.38' | 14114.8 | 2/2.8 | 0/0.5 | 1/0.3 | 2/0.5 |
| Multiple myeloma | 1.54' | 2.23' | 17/17.0 | 2/4.9 | 2/0.9 | 1/0.6 | 2/0.6 |
| Chronic lymphatic leukemia (CLL) | –0.34 | –0.45 | 6/5.6 | 1/2.1 | 2/0.6 | 0/0.3 | 0/0.4 |
| Leukemia excluding CLL | –0.81 | | 27/26.2 | 14/1 1.7 | 1/2.4 | 1/1.7 | 1/2.0 |
| Leukemia excluding CLL (2-y lag) | | –0.85 | 25/23.7 | 14/ 13.1 | 1/2.7 | 3/2.0 | 1/2.6 |
| All noncancer | –0.70 | –1.78 | 3,305/3.225.7 | 965/1,024.8 | 155/164.6 | 1091122.8 | 114/1 10.1 |
| Circulatory | –0.48 | –1.28 | 2,193/2,120.6 | 6421699.7 | 102/1 13.0 | 76183.6 | 81/77.0 |
| Respiratory excluding pneumonia | 0.10 | –0.16 | 194/208.2 | 96184.7 | 19/ 12.8 | 8/10.0 | 9/10.3 |
| Cirrhosis | 0.46 | 0.39 | 86188.0 | 22122.7 | 6/3.5 | 2/2.8 | 3/2.0 |
| External | –1.81 | –1.96 | 3741366.1 | 74175.9 | 11/13.5 | 11/9.9 | 2/6.6 |
| Person-years | | | 499,847 | 96,731 | 17,545 | 1 1,430 | 7,958 |

[a] The trend test statistic was calculated from individual doses. not the five exposure categories. It may be compared with a standard normal distribution to assess statistical significance. However, statistical significance may be exaggerated for diseases with a small number of deaths. See footnote d.

[b] Expected deaths were calculated from the experience of all workers in the study population, allowing for age, calendar year, gender, number of years monitored, and general socioeconomic category.

[c] The smoking-linked cancers were respiratory cancer, buccal cancer, and cancer of the esophagus, pancreas, and bladder.

[d] Based on computer simulations, the one-tailed p values associated with the trend test with a IO-y lag were estimated to be 0.065 for cancer of the pancreas, 0.038 for Hodgkin's disease, and 0.10 for multiple myeloma. For the 2-y lag, these $p$ values were estimated to be 0.056 for cancer of the liver, 0.026 for cancer of the pancreas, 0.029 for Hodgkin's disease, and 0.030 for multiple myeloma.

**Table 6.** Relative risks[a] (with 90% confidence limits) by external dose category for monitored Hanford Site workers employed at least 6 mo (based on a 2-y lag for leukemia and a 10-y lag for other categories).

| Dose category (mSv) | All cancer | All noncancer | Leukemia[b] | Multiple myeloma |
|---|---|---|---|---|
| 0– | 1.00 | 1.00 | 1.0 | 1.0 |
| 10– | 1.04 (0.9, 1.2) | 0.89 (0.8, 1.0) | 0.8 (0.4, 1.6) | 0.4 (0.1, 1.3) |
| 50– | 1.01 (0.8, 1.3) | 0.85 (0.7. 1.0) | 0.3 (0.03, 1.6) | 4.2 (0.7, 19) |
| 100– | 1.17 (0.9, 1.5) | 0.83 (0.7, 1.0) | 1.5 (0.4, 4.8) | 5.9 (0.5, 41) |
| 200– | 0.93 (0.7, 1.3) | 0.96 (0.8, 1.2) | 0.3 (0.02, 1.3) | 21 (2.1, 270) |

[a] The relative risks are the ratio of the risk for the indicated category relative to that of the lowest dose category (0–9 mSv).
[b] Excluding chronic lymphatic leukemia.

**Table 7.** Excess relative risk estimates with 90% confidence intervals for several cancer categories (based on a 2-y lag for leukemia and a 10-y lag for other categories).

| | Excess relative risk estimates [% (10 mSv)$^{-1}$] | |
|---|---|---|
| | 90% confidence intervals | 95% confidence intervals |
| All cancer | −0.1% (<0, 0.8%) | (<0, 1.0%) |
| Leukemia[a] | −1.1% (<0, 1.9%) | (<0, 3.6%) |
| All cancer except leukemia | −0.0% (<0, 1.0%) | (<0, 1.2%) |
| Digestive cancer | 1.1% (<0, 3.1%) | (<0, 3.7%) |
| Respiratory cancer | −0.0% (<0, 2.4%) | (<0, 3.0%) |
| Female breast cancer | −0.3% (<0, 27%) | (<0, 39%) |
| Other cancer | −0.9% (<0, 0.7%) | (<0, 1.1%) |
| All cancer in males | −0.1% (<0, 0.8%) | (<0, 1.0%) |
| All cancer in females | 0.1% (<0, 15%) | (<0, 20%) |
| Smoking-linked cancers[b] | 0.1% (<0, 1.8%) | (<0, 2.2%) |
| Other cancers | −0.3% (<0, 0.8%) | (<0, 1.1%) |

[a] Excluding chronic lymphatic leukemia.
[b] The smoking-linked cancers were respiratory cancer, buccal cancer, and cancer of the esophagus, pancreas, and bladder.

determine the sensitivity of analyses to these choices, analyses based on several alternative approaches were conducted. Risk estimates and confidence limits for all cancers are presented in Table 8; additional details for two of the approaches are presented in Tables 9 and 10.

Analyses in Tables 5–7 were based on the underlying cause of death as has been done in previous Hanford analyses and in most analyses of data from other nuclear worker studies. However, some recent analyses of worker data have included cancers noted on the death certificate but not considered to be the underlying cause of death (Wing et al. 1991; Kendall et al. 1992). It should be noted that the statistical methods used for these analyses are based on the assumption that the time of death is in some sense a surrogate for the time of tumor occurrence; this assumption may be less appropriate for cancers that are not considered to be the cause of death.

Analyses numbers 2, 10, and 12 in Table 8 were based on this alternative approach, while Table 9 presents additional detail. For these analyses, cancers (and cancers of specific types) were counted if indicated anywhere on the death certificate. Potentially [illegible] could contribute to the analyses of more than one cancer type; in fact, there were no instances where a death was included in more than one of the cancer subcategories included in Table 9. Note that Table 9 includes 159 more deaths in the all-cancer category than does Table 5.

The risk estimate for all-cancer remained negative with this approach. With a 10-y lag, the upper confidence limit was the same as that obtained when all cancers that were the underlying cause of death were included. There were no specific cancers that showed significant correlations that did not also show significant correlations in analyses based on the underlying cause of death. The risk estimate for leukemia (not shown in tables) was negative, with an upper confidence limit (two-sided 90% interval) of 1.5% per 10 mSv, comparable to the 1.9% value shown in Table 7.

Table 9 indicates two additional cases with multiple myeloma, one each in the top two dose categories. Both these deaths were reported in the 1989 paper but had not been included in formal statistical analyses. The addition of these two deaths led to a more significant correlation for multiple myeloma with both 10- and 10-y lags. Table 9 also shows three additional deaths with cancer of the pancreas (one each in the 0– and 50-mSv categories); these cases slightly increased the $p$ values for this disease. There were no deaths from Hodgkin's disease indicated on the death certificate but not considered to be the underlying cause of death. There was one such death with liver cancer, but it was in the lowest dose category and did not greatly change results from Table 5.

Analyses in Table 10 augment the analyses in Tables 5–7 by including deaths occurring in the State of Washington for the time period 1987–1989. Because of linkage with death files in the State of Washington, these deaths can be ascertained more quickly than those occurring in other states. The recent Washington deaths were included by using a proportional mortality approach, which is described in the 1989 paper. The methods used in this paper to obtain risk estimates and confidence limits are not appropriate for proportional mortality data and, therefore, risk estimates including these recent Washington deaths were not calculated.

Table 10 includes 127 cancer deaths that were not included in Tables 5–7. These additional deaths did

**Table 8.** Excess relative risk estimates (with 90% confidence limits) for all cancer based on several alternative analytic approaches (expressed as percent increase per 10 mSv).

| Analysis number | Modification in analytic approach[a] | Trend test statistics | Excess relative risk estimate (with 90% confidence limits) |
|---|---|---|---|
| Lag = 10 y | | | |
| 1. | None | –0.29 | **-0.15%(<0, 0.8%)** |
| 2. | Includes cancers indicated on death certificate, but not underlying cause | **-0.17** | -0.08% (<0, 0.8%) |
| 3. | Excludes dose received in construction work | –0.16 | –0.08%(<0, 0.9%) |
| 4. | Includes monitored workers employed <6 mo | **-0.42** | -0.21% (<0, 0.7%) |
| 5. | Excludes workers with confirmed internal depositions | 0.01 | 0.01%(<0, 1.1%) |
| 6. | No control for socioeconomic status | **0.73** | 0.39%(<0, **1.4%**) |
| 7. | No control for number of years monitored | –0.68 | –0.31% (<0, 0.5%) |
| 8. | No control for socioeconomic status or for number of years monitored | 0.23 | 0.11% (<0, **1.0%**) |
| Lag = 2 y | | | |
| 9. | None | –0.50 | –0.19% (<0, 0.5%) |
| 10. | Includes cancers indicated on death certificate, but not underlying cause | –0.29 | **–0.10%** (<0, 0.5%) |
| Lag = 20 y | | | |
| 11. | None | 0.57 | 0.56%(<0, 2.1%) |
| 12. | Includes cancers indicated on death certificate, but not underlying cause | 0.53 | 0.51% (<0, **2.1%**) |

[a] Except as indicated, analyses included all monitored workers employed at least 6 mo, included dose received in both operations and construction work, were based on deaths considered to be the underlying cause of death, and were controlled for age, calendar year, gender, number of years monitored (1-4 vs. 5+), and general socioeconomic category.

change the results for all cancers greatly, and no new statistically significant correlations for specific cancers evaluated in Table 5 resulted. However, the correlations for both cancer of the pancreas and multiple myeloma were strengthened with the inclusion of these additional deaths. There were five additional deaths from cancer of the pancreas including one in each of the two top dose categories, and four additional deaths from multiple myeloma, including one death in each of the three top dose categories. There were no deaths from Hodgkin's disease occurring in Washington State during the 1987–1989 time period.

Table 11 shows results of analyses that include cancers that were not the underlying cause of death and cancers occurring in the State of Washington during the time period 1987–1989 (including 16 deaths in this period where the underlying cause was not cancer). With a 10-y lag, this resulted in a $p$ value of 0.01 for multiple myeloma and a $p$ value of 0.06 for cancer of the pancreas.

Unlike most analyses presented in this paper, 1989 analyses did not include dose received in construction work but did include workers employed <6 mo. Analyses numbers **3** and **4** in Table **8** indicate that these changes do not greatly affect results; although, the risk estimate and upper confidence limit were slightly lower when very short-term workers were included. It is noted that the risk of cancer for workers employed <6 mo relative to workers employed longer was 1.28; for all causes of death, the comparable relative risk was **1.26.**

Excluding workers with confirmed internal depositions (analysis **5**) slightly increased both the estimate and the upper confidence limit. This exclusion also lessened the evidence of a correlation with external dose for cancer of the liver, as the liver cancer death with the highest dose also had a confirmed plutonium deposition; this death was discussed in our 1989 paper.

Analyses numbers 6, 7, and 8 show the effect of modifying the choice of controlling factors and indicate that not controlling for socioeconomic status increases

**Table 9.** Results of analyses of external dose for selected cancer categories in monitored workers employed at the Hanford Site for at least 6 mo including cancers noted on death certificate, but not considered to be the underlying cause of death. Except where noted, this is based on a 10-y lag.

| Cause of death | Trend test statistic[a] Exposure lagged for: 10 y | 2 y | Observed and expected deaths by exposure category (mSv) 0– Obs/Exp[b] | 10– Obs/Exp | 50– Obs/Exp | 100– Obs/Exp | 200+ Obs/Exp |
|---|---|---|---|---|---|---|---|
| All cancer | –0.17 | –0.29 | 1,079/1,082.1 | 3811377.7 | 69166.9 | 50149.6 | 46148.7 |
| Pancreas | 1.45[c] | 2.20[c] | 52154.0 | 20119.3 | 3/3.3 | 3/2.4 | 3/2.1 |
| Multiple myeloma | 2.50[c] | 2.95[c] | 17117.3 | 2/6.1 | 2/1.1 | 2/0.7 | 3/0.8 |
| Leukemia[d] | –0.98 | | 33/31.3 | 15/13.2 | 1/2.5 | 1/1.8 | 1/2.2 |
| Leukemia[d] (2-y lag) | | –1.01 | 31128.6 | 15114.6 | 1/2.8 | 3/2.1 | 1/2.8 |

[a] The trend test statistic was calculated from individual doses, not the five exposure categories. It may be compared with a standard normal distribution to assess statistical significance; however. statistical significance may be exaggerated for diseases with a small number of deaths. See footnote c.
[b] Expected deaths were calculated from the experience of all workers in the study population, allowing for age, calendar year. gender. number of years monitored, and general socioeconomic category.
[c] Based on computer simulations, the one-tailed p values associated with the trend test with a 10-y lag were estimated to be 0.080 for cancer of the pancreas and 0.023 for multiple myeloma. For the 2-y lag, these p values were estimated to be 0.032 for cancer of the pancreas and 0.007 for multiple myeloma.
[d] Excluding chronic lymphatic leukemia.

th risk estimate and upper confidence limits, while not controlling for number of years monitored has the opposite effect. Both variables can be demonstrated to affect cancer mortality, and thus we think that analyses that include adjustment for them (as in Tables 5–7) are less likely to be biased than analyses that do not include such adjustment.

Analyses number 9–12 show results based on 2- and 20-y lags. With the 20-y lag, the risk estimate was positive and the upper confidence limit higher, but the correlation did not approach statistical significance. Hodgkin's disease was the only cancer category exhibiting a statistically significant correlation with the 20-y lag. The correlation for multiple myeloma was in the negative direction with this lag; that for cancer of the pancreas was not close to statistical significance ($p = .17$).

Table 5 shows 86 deaths without cause-of-death information. For 44 cases, these were deaths for which certificates have not been located. After most analyses in this paper had been completed, it was discovered that 42 deaths had certificates that had not been submitted to the National Center for Health Statistics for assignment of the underlying cause of death. Of these, 33 were for deaths occumng in 1986.

Although nosologic codes for the underlying cause of death were not assigned by certified nosologists in these cases, death certificate text was manually reviewed for mention of cancer. Nine of the 42 certificates mentioned cancer, but in no case was leukemia, multiple myeloma, cancer of the pancreas, or Hodgkin's disease mentioned.

To examine whether or not the addition of these nine deaths might substantially alter the all-cancer risk estimate, an analysis including all cancers mentioned on the death certificate (as in Table 9 and analysis 2 - Table 8) was conducted. This modified the risk estima and confidence limits in Table 9 very little (the ris estimate was slightly increased from –0.08% to –0.0 per 10 mSv, and the upper confidence limit was al slightly increased from 0.77% to 0.82% per 10 mS Thus, it seems highly unlikely that the omission of thes deaths would have substantially modified results pre sented in this paper.

## DISCUSSION

Hanford workers continue to show a strong health worker effect with death rates from most causes su stantially below those of the general U.S. populatio Comparisons of death rates by radiation dose with the Hanford cohort show no evidence of a correlatio for all causes of death, all cancers, or leukemia wit radiation dose. These results are similar to those re ported in 1989 and are consistent with results fro other nuclear worker studies discussed in the 198 paper.

Since the 1989 paper was prepared. additiona reports of nuclear worker studies have been publishe (Beral et al. 1988; Wing et al. 1991; Kendallet al. 198 These newer reports also show death rates for mo causes that are substantially below national rates. a though leukemia death rates were found to be elevate in ORNL workers (Wing et al. 1991).

Dose-response analyses of workers at the U Atomic Weapons Establishment (AWE) (Beral et 1988) and of workers at ORNL show statistically sig nificant correlations for all cancer and risk estimat that are several times those obtained from extrapolatio from high-dose data. Data on Hanford workers clear

**Table 10.** Results of analyses of external dose for selected cancer categories in monitored workers employed at the Hanford Site for at least 6 mo, including cancers occumng in the state of Washington from 1987–1989. Except where noted, this is based on a 10-y lag.

| Cause of death | Trend test statistic? Exposure lagged for: 10 y | 2 y | Observed and expected deaths by exposure category (mSv) e Obs/Exp[b] | 10– Obs/Exp | 50– Obs/Exp | 100– Obs/Exp | 200+ Obs/Exp |
|---|---|---|---|---|---|---|---|
| All cancer | -0.20 | -0.38 | 1,023/1.031.5 | 3921381.4 | 70/71.1 | 56153.2 | 52/55.8 |
| Pancreas | 1.91' | 2.57' | 54155.4 | 19119.4 | 2/3.6 | 4/2.4 | 4/2.2 |
| Multiple myeloma | 1.99' | 2.90[c] | 18/18.2 | 2/6.3 | 3/1.3 | 2/1.0 | 3/1.2 |
| Leukemia[d] | -0.78 | | 29127.8 | 15/13.2 | 1/2.7 | 2/1.9 | 1/2.3 |
| Leukemia[d] (2-y lag) | | -0.84 | 27125.2 | 15/14.7 | 1/3.0 | 4/2.2 | 1/2.9 |

[a] The trend test statistic was calculated from individual doses, not the five exposure categories. It may be compared with a standard normal distribution to assess statistical significance; however, statistical significance may be exaggerated for diseases with a small number of deaths. See footnote c.
[b] Expected deaths were calculated from the experience of all workers in the study population, allowing for age, calendar year, gender, number of years monitored, and general socioeconomic category.
[c] Based on computer simulations, the one-tailed $p$ values associated with the trend test with a 10-y lag were estimated to be **0.033** for cancer of the pancreas and **0.040** for multiple myeloma. For the 2-y lag, these $p$ values were estimated to be **0.019** for cancer of the pancreas and 0.011 for multiple myeloma.
[d] Excluding chronic lymphatic leukemia.

**Table 11.** Results of analyses of external dose for selected cancer Categories in monitored workers employed at the Hanford Site for at least 6 mo including cancers occurring in the state of Washington from 1987–1989, and including cancers noted on the death certificate, but not considered to be the underlying cause of death. Except where noted, this is based on a 10-y lag.

| Cause of death | Trend test statistic' Exposure lagged for: 10 y | 2 y | Observed and expected deaths by exposure category (mSv) 0– Obs/Exp[b] | 10– Obs/Exp | 50– Obs/Exp | 100– Obs/Exp | 200+ Obs/Exp |
|---|---|---|---|---|---|---|---|
| All cancer | 0.05 | -0.04 | 1,131/1.135.3 | 4341431.7 | 82179.3 | 61/59.1 | 60162.5 |
| Pancreas | 1.61' | 2.28' | 56157.1 | 20120.9 | 3/3.9 | 4/2.6 | 4/2.5 |
| Multiple myeloma | 2.67' | 3.45' | 18/18.6 | 2/7.5 | 3/1.5 | 3/1.1 | 4/1.4 |
| Leukemia[d] | -0.94 | | 35132.8 | 16/14.8 | 1/2.9 | 212.0 | 1/2.5 |
| Leukemia[d] (2-y lag) | | -0.99 | 33130.2 | 16/16.2 | 1/3.2 | 4/2.3 | 1/3.1 |

'The trend statistic was calculated from individual doses, not the five exposure categories. It may be compared with a standard normal distribution to assess statistical significance: however, statistical significance may be exaggerated for diseases with a small number of deaths. See footnote c.
[b] Expected deaths were calculated from the experience of all workers in the study population, allowing for age, calendar year, gender, number of years monitored, and general socioeconomic category.
[c] Based on computer simulations, the one-tailed $p$ values associated with the trend test with a 10-y lag were estimated to be **0.062** for cancer of the pancreas and 0.011 for multiple myeloma. For the 2-y lag, these $p$ values were estimated to be **0.028** for cancer of the pancreas and **0.003** for multiple myeloma.
[d] Excluding chronic lymphatic leukemia.

:o not support the high-risk estimates obtained from ORNL and **AWE** data. The Hanford-based upper con-idence limit of about 1% per 10 mSv is well below the stimates of 7.6% **(AWE)** and **3.3%** (ORNL) obtained rom these studies with a 10-y lag, and estimates at this evel can be strongly rejected ($p < .001$) with the Han-ord data. The ORNL estimate of 4.9%, obtained with a 20-y lag, can also be strongly rejected ($p < .001$) when Hanford data are analyzed with this lag.

However, the **AWE** and ORNL risk estimates carry arg uncertainties, and the three studies may not be inconsistent with one another. Confidence limits based on the **AWE** data are presented by Beral et al. (1988) while confidence limits based on the ORNL data are given in Gilbert (1992). Combined analyses of Hanford and ORNL data are currently underway and will address this question more rigorously. Combined international analyses are also being conducted (Cardis and Kaldor 1989).

The **AWE** correlation resulted primarily from a correlation for lung cancer, and nonmalignant respiratory disease showed a similar correlation. The ORNL

correlation was also strongest in cancers that have been linked with smoking (Gilbert 1992). Thus, a smoking-related bias may have contributed to these correlations. Although the ORNL study found an excess of leukemia in comparison to the **U.S.** population, leukemia was not found to be correlated with occupational radiation dose in either AWE or ORNL workers. The total person-Sv for AWE workers was 73 while that for ORNL workers was 144, compared with 861 person-Sv received by Hanford workers. In terms of total person-Sv, both the AWE and ORNL studies are quite small compared to those reported in other studies such as Hanford, UK Atomic Energy Facility with 660 person-Sv (Beral et al. 1985), and the Sellafield Plant with 1,250 person-Sv (Smith and Douglas 1986).

Kendall et al. (1992) reported a weak positive association with radiation dose for all cancers (one-tailed $p = .10$) and a stronger association for leukemia ($p = .06$) in the UK National Registry for Radiation Workers (NRRW). Risk estimates for both disease categories were higher than those obtained through extrapolation from high-dose data, but confidence intervals indicated consistency with high-dose predictions. The Hanford-based confidence limits include the NRRW all-cancer risk estimate. The NRRW leukemia risk estimate was higher than the Hanford-based upper confidence limit, but leukemia confidence limits for the two studies overlap. The NRRW study includes many of the same workers evaluated in the AEA, AWE, and Sellafield populations. The total person-Sv for NRRW workers was 3,200; nearly four times that for Hanford.

In previous analyses of the Hanford data, multiple myeloma was the cancer most strongly linked with radiation dose. The one-tailed $p$ value obtained in the analyses presented in Table 5 with a 10-y lag was 0.10, compared with a $p$ value of 0.002 obtained in comparable analyses based on data through 1981, and published in 1989. Ten of the 23 deaths shown in Table 5 occurred between 1982 and 1986, with one each in the 50–99 mSv and 200+ mSv categories. One death in the 200+ mSv category occurred in the state of Washington and had been included in 1989 supplementary analyses including recent Washington deaths. A test for consistency in results before and after 31 December 1981 yielded a $p$ value between 0.1 and 0.2.

However, significant correlations were obtained a) when analyses were expanded to include deaths with multiple myeloma listed on the death certificate but not considered to be the underlying cause ($p = .02$); b) when analyses were expanded to include deaths occurring in Washington State in the time period 1987–1989 ($p = .04$); or c) when a 2-y latency period (instead of 10-y) was assumed ($p = .03$). When a) and b) are combined. the $p$ value was 0.01. However, none of these correlations is as striking as that observed earlier and could be interpreted as spurious given the large number of disease categories examined. Furthermore, the approaches used in analyses presented in Tables 8, 9, and 10 may be particularly subject to bias. For example, the multiple myeloma correlation in Hanford workers has been widely publicized, and it is possible that a multiple myeloma that was not the cause of death would be more likely to be noted on the death certificate of a worker known to be a radiation worker than for other workers.

Nevertheless, the continued appearance of multiple myeloma deaths in Hanford workers with high doses argues against readily dismissing this finding. The NRRW study just noted also shows a correlation for multiple myeloma ($p = .06$), which largely resulted from Sellafield workers included in the study, for whom a correlation had been previously reported (Smith and Douglas 1986). Multiple myeloma has also been clearly linked with radiation dose in A-bomb survivors, although the magnitude of the risk estimate would not lead to the expectation of a correlation at low doses (Shimizu et al. 1990).

With a 2-y lag, cancer of the pancreas showed a significant correlation with radiation dose in Hanford analyses based on data through 1 April 1974 (Gilbert and Marks 1979) and on data through 1 May 19[illegible] (Gilbert and Marks 1980). However, the correlation did not approach statistical significance with a 10-y lag in these earlier analyses. In later analyses, including data through 1978 (Tolley et al. 1983) and through 198[illegible] (Gilbert et al. 1989a), the correlation had declined to nonsignificant levels. Analyses in this paper indicate a correlation for cancer of the pancreas that was statistically significant with the 2-y lag (one-tailed $p = .01$) and that approached statistical significance with the 10-y lag ($p = .07$). Results were similar with the addition of cancers not considered to be the underlying cause of death, of cancers occumng in the state of Washington in the time period 1987–1989, or of both.

Death certificate diagnosis of cancer of the pancreas is known to be inaccurate. It was discovered earlier that one of the high-dose deaths in the Hanford analyses was probably due to cancer of the stomach (Gilbert and Marks 1980). Removal of this death would reduce the evidence for a correlation. For consistency, **all** deaths are categorized according to information on the death certificate and, thus, this death has remained in the cancer of the pancreas category.

Evidence for radiation-induced cancer of the pancreas was reviewed by the BEIR **V** Committee (National Academy of Science 1990, p. 334), who summarized their conclusions as follows:

> An association between cancer of the pancreas and previous irradiation, suggested by several reports in the past, has not been confirmed in more recent and thorough studies of irradiated human populations. The pancreas appears, therefore. to be relatively insensitive to radiation carcinogenesis. . . .

Cancer of the pancreas was not among the sites for which the ICRP (1991) provided estimates and weighing factors and has not been linked with radiation exposure in nuclear workers studies other than Han-

ford. Because there is clearly no strong ***a priori*** reason for expecting a correlation for cancer of the pancreas but not other types of cancer, it seems appropriate to interpret the Hanford finding as probably spurious.

The correlation observed for Hodgkin's disease is even more likely to represent a spurious finding. The BEIR **V** report (National Academy of Science 1990, p. 329) devotes a single sentence to this disease, stating that "For Hodgkin's disease, the data are reasonably consistent in showing no excess in irradiated populations." Hodgkin's disease has not shown a correlation with radiation exposure in any of the other nuclear worker studies.

A major objective of studies of nuclear workers is to provide a direct evaluation of effects of exposure at low doses and dose rates for comparison with risk estimates that have been recommended for use in radiation protection, for example, estimates provided by the International Commission on Radiological Protection (1991) and by the National Academy of Science's BEIR **V** Committee (1990). These risk estimates have been obtained by extrapolation from data on populations exposed at high doses, such as the Japanese A-bomb survivors.

The ICRP based its lifetime risk estimates for leukemia and all-cancer except leukemia on risk estimates presented in a report of the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR 1988). Based on analyses of Japanese A-bomb survivor data, UNSCEAR presents linear excess relative risk coefficients for leukemia of **3.7%** and 3.8% per 10 mSv for males and females, respectively, exposed in adulthood. The comparable coefficients for all cancer except leukemia were 0.24% and 0.46% for males and females, respectively, exposed in adulthood. For exposure received at low doses and dose rates, the ICRP recommended reducing the estimates provided by UNSCEAR by a factor of 2.

For leukemia, the risk estimate based on Hanford data (see Table **7)** was negative and the confidence limits included zero, indicating that the possibility of no risk at low doses and dose rates cannot be excluded. With the 90% interval, the upper confidence limit of 1.9% per 10 mSv is about one-half the linear estimate presented in UNSCEAR and indicates that a risk estimate $\geq 1.9\%$ can be rejected at the 0.05 level. This result could be interpreted as indicating that the revised ICRP model probably has not seriously underestimated leukemia risks.

For all cancer except leukemia, the Hanford-based estimate was again negative. The upper confidence limit of 1.0% per 10 mSv was about four times the UNSCEAR coefficient for males and about eight times the estimate reduced by the factor of **2** recommended by the ICRP. To account for the larger UNSCEAR risk coefficient for females, we performed an analysis in which risks were expressed as multiples of the UNSCEAR model and which involved weighting doses received by females by a factor $0.46/0.24 = 1.92$ times doses received by males. This analysis also yielded an upper limit about four times the UNSCEAR prediction (or eight times the ICRP prediction).

We also analyzed the Hanford data for consistency with predictions of the models recommended by the BEIR **V** Committee (National Academy of Science 1990). The BEIR **V** models incorporate dependencies of the excess relative risk on age at exposure, time after exposure, and gender, and were primarily based on analyses of the Japanese A-bomb survivor data (although the female breast cancer model used other data sets). Separate models were determined for leukemia, digestive cancer, respiratory cancer, female breast cancer, and other cancers. Hanford data were analyzed by expressing estimates and confidence limits as multiples of risks predicted under the BEIR **V** models, and this involved weighting each annual dose according to age, time from the effect, and gender. All cancers except leukemia .were analyzed in combination and, in this case, the model involved weighting by the type of cancer as well.

Using this approach, the leukemia risk estimate was –0.6 times the BEIR **V** predictions, and the upper confidence limit (two-sided 90% interval) was 0.8 times the BEIR **V** predictions. The BEIR V leukemia model included reduction of **risks** by a factor of **2** for low doses; thus, this result is very similar to the result previously noted for the ICRP model. For all cancers except leukemia, the risk estimate was almost exactly zero and the upper confidence limit was 1.5 times BEIR **V** predictions based on a linear model with no reduction for low dose rates. The factor of 1.5 is smaller than the factor of 4 resulting from comparison with UNSCEAR 1988 linear estimates. This difference results primarily because the BEIR **V** respiratory cancer model predicts large risks in workers; this occurs because the BEIR V model transports a relative risk coefficient from the Japanese A-bomb survivors where baseline risks for respiratory cancer are low, and because the model includes a decline with time since exposure and assigns the highest risks to the time period when workers are receiving most of their exposure.

The confidence limits just discussed do not include uncertainty resulting from unidentified confounding factors that may have biased results or uncertainty in the dose estimates used in the study. In particular, the recorded dose may overestimate bone marrow dose and doses to other organs, which have been the basis of risk estimates obtained from recent analyses of Japanese A-bomb survivor data. A detailed evaluation of Hanford historical dosimetry has recently been conducted (Wilson et al. 1990). Further work to evaluate the relationship of recorded dose and doses to various organs, and to examine the effect of dosimetry biases and uncertainties on dose-response analyses, is planned.

Current data from Hanford indicate that low-level radiation exposure risks are consistent with no risk, with predictions by the ICRP or BEIR **V,** and with risks that are several times these predictions. These results

appear to be consistent with those of most other nuclear worker studies, but two studies of much smaller cohorts have indicated that risks may be larger than predictions based on high-dose data. In order to obtain the best assessment of data from all occupational studies, it is important to conduct analyses based on combined data. Analyses of combined U.S. data, which will update results in Gilbert et al. (1989b), are in progress. Combined analyses of international data from the U.S., UK, and Canada are also underway with the International Agency for Research on Cancer serving as the coordinating agency (Cardis and Kaldor 1989).

**Acknowledgements—This work was supported by the U.S. Department of Energy under contract DE-AC06-76RLO-1830. The authors acknowledge the vital statistics offices of the individual states as the source of death record data and appreciate the offices' technical support of this research. The authors are solely responsible for the data analyses and the interpretation of the results.**

## REFERENCES

Beral, V.; Fraser, P.; Carpenter, L.; Booth, M.; Brown, A.; Rose, G. Mortality of employees of the Atomic Weapons Establishment, 1951–1982. Br. Med. J. 297:757–770; 1988.

Beral, V.; Inskip, H.; Fraser, P.; Booth, M.; Coleman, D.; Rose, G. Mortality of employees of the United Kingdom Atomic Energy Authority, 1946–1979. Br. Med. J. 291:440–447; 1985.

Bureau of the Census. Alphabetical index of industries and occupations, 1970 census of the population. Washington, DC: U.S. Government Printing Office; 1971.

Cardis, E.; Kaldor, J. Protocol of combined analyses of cancer mortality among nuclear industry workers. Lyon, France: International Agency for Research on Cancer (IARC); Internal Report No. 89/005; 1989.

Doll, R.; Peto, R. The causes of cancer. New York Oxford Medical Publications, Oxford University Press; 1981.

Gilbert, E. S. Issues in analyzing the effects of occupational exposure to low levels of radiation. Statistics Med. 8:173–187; 1989.

Gilbert, E. S. Studies of workers exposed to low doses of external radiation. In: Occupational medicine: State of the art reviews. Vol. 6, No. 4, October-December 1991. Philadelphia: Hanley & Belfus, Inc.; 1991:665–680.

Gilbert, E. S. Mortality of workers at the Oak Ridge National Laboratory. Health Phys. 62:260–261; 1992.

Gilbert, E. S.; Buchanan, J. A. An alternative approach to analyzing occupational mortality data. J. Occupational Med. 26:822–828; 1984.

Gilbert, E. S.; Marks, S. An analysis of the mortality of workers in a nuclear facility. Radiat. Res. 79:122–148; 1979.

Gilbert, E. S.; Marks, S. An updated analysis of mortality of workers in a nuclear facility. Radiat. Res. 83:740–741; 1980.

Gilbert, E. S.; Buchanan, J. A.; Holter, N. A. Description of the process used to create 1992 Hanford mortality study database. Richland, WA: Pacific Northwest Laboratory; Report No. PNL-8449; 1992.

Gilbert, E. S.; Petersen, G. R.; Buchanan, J. A. Mortality of workers at the Hanford site: 1945–1981. Health Phys. 56:11–25; 1989a.

Gilbert, E. S.; Fry, S. A.; Wiggs, L. D.; Voelz, G. L.; Cragle, D. L.; Petersen, G. R. Analyses of combined mortality data on workers at the Hanford Site, Oak Ridge National Laboratory, and Rocky Flats Nuclear Weapons Plant. Radiat. Res. 120:19–35; 1989b.

International Commission on Radiological Protection. Recommendations of the International Commission on Radiological Protection. ICRP Publication 60; Ann. ICRP 21:1–201; 1991.

Kendall, G. M.; Muirhead, C. R.; MacGibbon, B. H.; O'Hagan, J. A.; Conquest, A. J.; Goodill, A. A.; Butland, B. K.; Fell, T. P.; Jackson, D. A.; Webb, M. A.; Haylock, R. G. E.; Thomas, J. M.; Silk, T. J. Mortality and occupational exposure to radiation: First analysis of the National Registry for Radiation Workers. Br. Med. J. 304:220–225; 1992.

Mantel, N.; Haenszel, W. Statistical aspects of the analysis of data from retrospective studies of disease. JNCI 22:719–748; 1958.

Monson, R. R. Analysis of relative survival and proportional mortality. Computer Biomedical Res. 7:325–332; 1974.

National Academy of Sciences. Committee on the Biological Effects of Ionizing Radiation (BEIR V). Health effects of exposure to low levels of ionizing radiation. Washington, DC: National Academy Press; 1990.

Shimizu, Y.; Kato, H.; Schull, W. J. Studies of mortality of A-bomb survivors. 9. Mortality, 1950–1985: Part 2. Cancer mortality based on the recently revised doses (DS86). Radiat. Res. 121:120–141; 1990.

Smith, P. G.; Douglas, A. J. Mortality of workers at the Sellafield plant of British Nuclear Fuels. Br. Med. J. 293:845–52; 1986.

Tolley, H. D.; Marks, S.; Buchanan, J. A.; Gilbert. E. S. A further update of the analysis of mortality of workers at a nuclear facility. Radiat. Res. 95:211–213; 1983.

United Nations Scientific Committee on the Effects of Atomic Radiation. Sources, effects, and risks of ionizing radiation: Report to the General Assembly, with annexes. New York: United Nations; 1988.

Wilson, R. H.; Fix, J. J.; Baumgartner, W. V.; Nichols. L. J. Description and evaluation of the Hanford personnel dosimeter program from 1944 through 1989. Richland. WA: Pacific Northwest Laboratory; Report No. PNL-7447; 1990.

Wing, S.; Shy, C. M.; Wood, J. L.; Wolf, S.; Cragle. D. L.; Frome, E. L. Mortality among workers at Oak Ridge National Laboratory: Evidence of radiation effects in follow-up through 1984. J. Am. Med. Assoc. 265:1397–1402; 1991.

World Health Organization. International classification of disease. 8th Rev. Geneva: WHO; 1965.