



## Original Contribution

# Leukemia Mortality among Workers at the Savannah River Site

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Received for publication January 29, 2007; accepted for publication May 11, 2007.

The authors investigated associations between ionizing radiation and leukemia mortality among workers at the Savannah River Site (South Carolina). A total of 18,883 workers hired between 1950 and 1986 were followed through 2002 to ascertain causes of death. Estimates of radiation doses from external sources and internal tritium uptakes were derived from dosimetry records through 1999. Radiation dose–mortality trends were evaluated for leukemia, leukemia excluding chronic lymphocytic leukemia, and myeloid leukemia. A positive association was observed between leukemia mortality and radiation dose under a 3-year lag assumption (excess relative rate/10 mSv = 0.04, 90% confidence interval: –0.00, 0.12). The association was of larger magnitude for leukemia excluding chronic lymphocytic leukemia (excess relative rate/10 mSv = 0.08, 90% confidence interval: 0.01, 0.20) and myeloid leukemia (excess relative rate/10 mSv = 0.12, 90% confidence interval: 0.02, 0.35). Compared with males, females had less complete dosimetry information; when analyses were restricted to males, the estimated association for each cause of death increased slightly in magnitude and goodness of fit. Exposures accrued 3–15 years prior were more strongly related to leukemia than exposures in the more distant past. This study provides evidence of positive associations between radiation dose and leukemia mortality among Savannah River Site workers. The temporal patterns of association appear consistent with those in studies of populations exposed at higher dose rates.

leukemia; mortality; nuclear energy; radiation, ionizing; South Carolina

Abbreviations: CI, confidence interval; CLL, chronic lymphocytic leukemia; ERR, excess relative rate; ICD, *International Classification of Diseases*.

To our knowledge, the largest study to date of cancer in workers in the nuclear industry assessed mortality among workers in 155 nuclear facilities in 15 countries (1). In that study, the estimated association between leukemia mortality and cumulative radiation dose under a 2-year exposure lag assumption was smaller in magnitude than an estimate obtained by fitting a linear dose–response model to male atomic bomb survivors exposed between the ages of 20 and 60 years; 90 percent confidence limits ranged from less than zero to more than twice the linear estimate for A-bomb survivors (excess relative rate (ERR)/10 mSv = 0.02, 90 percent confidence interval (CI): <0, 0.07). The temporal pattern of the radiation dose–leukemia association in the

15-country study is noteworthy, because the nuclear workers' data showed evidence of an increase in the magnitude of the radiation–leukemia association with increasing lag assumptions (1); in contrast, evidence of radiation effects diminished with time since exposure in many studies of leukemia among people who have received high dose-rate exposures (2).

Although pooling nuclear worker data affords the opportunity for statistical precision, a potential disadvantage of such an approach is that it increases the possibility of heterogeneity in exposure effects between cohorts and/or heterogeneity in selection or confounding factors and measurement of exposure and outcome. From this perspective,

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analyses of a single cohort of workers may be useful if such analyses suffer less bias than pooled analyses yet still encompass adequate numbers of cases to draw valid statistical inferences. In this paper, we assess radiation dose–leukemia associations in a large cohort of US nuclear weapons workers that is independent of the 15-country study. Although our study includes only about one third the number of leukemias included in the 15-country study, the number of cases exceeds the number contributed by any single cohort in the collaborative study and is comparable to the number of leukemia cases contributed by the United Kingdom, by the 13 countries other than the United States and the United Kingdom, or by the combined Hanford, Oak Ridge National Laboratory, and US commercial nuclear power cohorts included in the 15-country study (1).

In this paper, we evaluate associations between ionizing radiation and mortality due to leukemia among workers employed at the Savannah River Site. We focus on ionizing radiation doses from external sources and internal doses from tritium intakes. We examine modification of radiation dose–leukemia associations by subtype of leukemia and time since exposure.

## MATERIALS AND METHODS

The Savannah River Site, located near Aiken, South Carolina, was constructed in 1950 by E. I. du Pont de Nemours and Company (DuPont) to produce materials for the US nuclear weapons program. Activities at the Savannah River Site have included operation of five large reactors, two chemical separation areas, a heavy-water extraction plant, and nuclear fuel and target fabrication plants, as well as test reactors, power plants, and laboratories.

Between 1950 and 1986, 21,204 people were known to have been hired by DuPont to work at the Savannah River Site. We excluded from these analyses workers for whom date of birth ( $n = 57$ ), sex ( $n = 10$ ), or date of hire ( $n = 184$ ) was unknown. People employed less than 90 days ( $n = 1,355$ ) were excluded since short-term workers often differ from those with longer employment tenures with respect to mortality risk and cumulative occupational exposures (3). Workers known to be employed at other US Department of Energy facilities ( $n = 715$ ) also were excluded because we did not collect information on occupational radiation exposures that occurred outside of employment at the Savannah River Site. Vital status and cause of death were ascertained through December 31, 2002, via records of the Social Security Administration and the National Death Index. We obtained underlying and contributing causes of death for deceased workers. For deaths occurring prior to 1979, cause-of-death information was coded according to the Eighth Revision of the *International Classification of Diseases* (ICD); for deaths occurring in 1979 or later, cause of death information was coded to the ICD revision in effect at the time of death. If there was no death indication for a worker and he or she was confirmed to be alive on January 1, 1979, or later by the Social Security Administration or the Savannah River Site's employment records, then that worker was assumed to be alive as of December 31, 2002.

We conducted dose-response analyses for leukemia (ICD-8 codes 204–207, ICD-9 (Ninth Revision) codes 204–208, ICD-10 (Tenth Revision) codes C91–95), leukemia excluding chronic lymphocytic leukemia (CLL; ICD-8 and ICD-9 code 204.1, ICD-10 codes C91.1 and C91.4), and myeloid leukemia (ICD-8 and ICD-9 code 205, ICD-10 code C92). We used information on all listed causes of death (underlying and contributory) to define the outcome categories. The use of multiple-cause-of-death information may be particularly valuable as a way to increase the sensitivity and specificity of case classifications for studies of diseases, such as adult leukemia, that tend to occur at older ages in patients with multiple morbid conditions at death (4).

The exposure of interest was defined as cumulative whole-body radiation dose equivalent in milliSieverts (mSv) from external sources and tritium received during employment at the Savannah River Site. Personal monitoring data were available for the period 1950–1999 from Savannah River Site records. Monitoring of external ionizing radiation exposure began with film badge dosimeters as well as neutron nuclear track emulsion dosimeters; beginning in 1970, external exposures were monitored via thermoluminescent dosimeters. Radiation dose estimates from tritium depositions were derived via bioassay monitoring. Details about the Savannah River Site's dosimetry program, including the quality factors used to calculate dose equivalents, have been reported previously (5–7). Whole-body radiation doses were estimated for work-years in which dose data were missing by using dose estimates in adjacent time periods and average values for similar workers. Estimated annual doses constituted 4 percent of employment years for males and 17 percent of employment years for females (7).

Analyses were conducted by using a nested case-control approach. Risk sets were formed by incidence density matching of cases (leukemia deaths) to noncases. Risk sets were matched on the following factors: attained age; sex; race (Black vs. other); year of birth (born before 1915; in 1915–<1925, 1925–<1930, 1930–<1935, or 1935–<1950; or after 1950); pay code (used to control for socioeconomic differences in mortality and classified on the basis of the worker's pay schedule when hired as paid monthly, weekly, or hourly); and employment status (used to control for the healthy worker survivor effect and to indicate whether a worker was employed) (8–10). All eligible controls were selected for each case. Index dates for cases and controls were defined as their date of death (for a case) or date of selection (for a control). Cumulative radiation dose was examined under a fixed 3-year lag and in time windows defined by the periods 3–<15, 15–<30, and  $\geq 30$  years prior to the index date. Since exposure data were available for the period 1950–1999 while follow-up spanned the period 1950–2002, a 3-year lag was the minimal lag assumption evaluated in these analyses. The statistical program PECAN was used to fit conditional logistic regression models of the form  $RR \cong OR = e^{\alpha_i} (1 + \beta x)$ , where  $\alpha_i$  indexes the stratum-specific risk sets and  $x$  represents cumulative dose (in 10-mSv units) (11). This approach is equivalent to a Cox proportional hazards regression analysis with age as the time scale and stratification on sex, race, birth cohort, pay code, and employment status (12, 13). The value  $\beta$  provides

an estimate of the ERR per 10-mSv dose and is discussed as such in this paper. Confidence intervals were estimated via the likelihood method. Goodness of fit was evaluated by a likelihood ratio test comparing nested models.

Because radiation monitoring records were less complete for female than for male workers (suggesting greater potential for exposure misclassification for female than for male workers) and the majority of the dose was accrued by male workers, we also conducted analyses by using data for the subcohort of 15,264 male workers. Given the low doses and small number of leukemia deaths among female workers, we did not estimate separate dose-response trends for females.

## RESULTS

With follow-up through 2002, we found that 27 percent of the study cohort was deceased (5,098 workers), 72 percent of the cohort was alive at the end of follow-up (13,590 workers), and 1 percent of the cohort was lost to follow-up (195 workers). Information on cause of death was collected for 99 percent of decedents (5,047 workers). In total, 84 leukemia deaths were observed, of which 73 were cases for whom leukemia was listed as the underlying cause of death. Acute myeloid leukemia accounted for 29 cases, chronic myeloid leukemia for 10 cases, acute lymphocytic leukemia for four cases, and CLL for 22 cases; the remainder consisted of monocytic leukemia ( $n = 2$ ) and other and unspecified leukemias ( $n = 17$ ).

The analyses involved risk sets formed by density sampling; the average risk set included 480 controls, the median number of controls per risk set was 451, and the smallest risk set included one case and four controls. The distributions of cases by study factors are shown in table 1. The average age of leukemia cases was 63.7 years, with the majority born prior to 1930 (table 1). Consistent with the relatively old age of cases, 72 of the 84 leukemia cases were hired prior to 1960. The mean cumulative dose under a 3-year lag accrued by males was 43.7 mSv (standard deviation, 73.4), and the mean dose accrued by females was 4.9 mSv (standard deviation, 14.9).

Under the minimal 3-year lag assumption, the estimated ERR of leukemia was 0.041 per 10 mSv (90 percent CI: -0.001, 0.116). The estimate of association between ionizing radiation dose and leukemia excluding CLL was of larger magnitude than the estimated association for all leukemias (ERR/10 mSv = 0.077, 90 percent CI: 0.014, 0.198). When analyses were restricted to myeloid leukemias, the magnitude and fit of the model were greater (ERR/10 mSv = 0.123, 90 percent CI: 0.021, 0.354), although the analyses of myeloid leukemia deaths were based on smaller numbers of cases.

Table 2 also shows the results of analyses restricted to male workers. For each leukemia category, there was a modest increase in the magnitude of association and goodness of model fit upon exclusion of female workers. For example, among male Savannah River Site workers, the association between radiation dose and mortality due to leukemia excluding CLL was ERR/10 mSv = 0.082 (90 percent CI: 0.016, 0.211).

**TABLE 1. Distribution of cases with respect to attained age, sex, race, pay code, birth cohort, employment status, and subtypes of leukemia at the Savannah River Site, South Carolina, 1950–2002**

	Leukemia	Leukemia (excluding CLL*)	Myeloid leukemia
Mean age in years	63.7 (11.7)†	63.7 (12.2)	64.0 (11.5)
Sex			
Male	79	58	37
Female	5	4	3
Race			
White/other	79	60	39
Black	5	2	1
Pay code			
Monthly	22	18	15
Weekly	16	11	7
Hourly	46	33	18
Birth cohort			
<1915	7	5	4
1915–<1925	35	27	19
1925–<1930	24	18	9
1930–<1935	8	5	3
1935–<1950	6	3	2
≥1950	4	4	3
Employment status			
Employed	13	10	7
Terminated	71	52	33
Total	84	62	40

\* CLL, chronic lymphocytic leukemia.

† Values in parentheses, standard deviation.

ERRs for three time windows are shown in table 3. Associations between radiation and leukemia mortality under the 3-year lag were largely due to doses accrued in the period 3–<15 years prior to the index date. A positive association of lower magnitude was observed in the period 15–<30 years prior, and essentially no association with radiation doses accrued in the period ≥30 years prior (table 3). For leukemia excluding CLL and myeloid leukemia, a positive but highly imprecise association was observed with doses accrued ≥30 years in the past. In analyses restricted to males (table 3), similar patterns were observed, with some improvement in the precision of estimates when contrasted to analyses that included males and females. Exposures accrued in the time window 3–<15 years prior to the index date were positively associated with mortality due to leukemia (ERR/10 mSv = 0.280, 90 percent CI: 0.021, 0.728), leukemia excluding CLL (ERR/10 mSv = 0.369, 90 percent CI: 0.003, 1.046), and myeloid leukemia (ERR/10 mSv = 0.437, 90 percent CI: <0, 1.598).

Table 4 shows the distribution of observed leukemia deaths and estimates of relative rates by categories of cumulative dose under a 3-year lag assumption derived via a model that included eight indicator terms for these nine dose categories (results tabulated by categories of

**TABLE 2. Estimated association between cumulative radiation dose (under a 3-year lag assumption) and mortality due to leukemia among workers at the Savannah River Site, South Carolina, 1950–2002**

	Leukemia	Leukemia excluding CLL*	Myeloid leukemia
Males and females			
ERR*/10 mSv	0.041	0.077	0.123
90% CI*	−0.001, 0.116	0.014, 0.198	0.021, 0.354
Likelihood ratio test ( $\chi^2$ , 1 df)	2.50	4.92	5.14
Males only			
ERR/10 mSv	0.044	0.082	0.136
90% CI	0.000, 0.123	0.016, 0.211	0.025, 0.395
Likelihood ratio test ( $\chi^2$ , 1 df)	2.72	5.22	5.54

\* CLL, chronic lymphocytic leukemia; ERR, excess relative rate; CI, confidence interval.

cumulative dose accrued in the period 3–<15 years prior are presented in Appendix table 1). In analyses of all leukemias, the estimated rate ratios increased monotonically across

nearly all categories of dose with the exception of the dose category 5–<10 mSv (for which the estimated rate ratio was similar to that for the category >0–<5 mSv) and the

**TABLE 3. Estimated association between mortality due to leukemia and cumulative radiation dose accrued by workers in three exposure time windows, Savannah River Site, South Carolina, 1950–2002**

Time since exposure	Leukemia	Leukemia excluding CLL*	Myeloid leukemia
Males and females			
3–<15 years			
ERR*/10 mSv	0.265	0.344	0.403
90% CI*	0.015, 0.694	−0.004, 0.980	<0, 1.441
Likelihood ratio test	3.18	2.61	1.65
15–<30 years			
ERR/10 mSv	0.011	0.008	0.007
90% CI	<0, 0.105	<0, 0.1595	<0, 0.327
Likelihood ratio test	0.07	0.01	0.00
≥30 years			
ERR/10 mSv	−0.004	0.100	0.209
90% CI	<0, 0.145	<0, 0.440	<0, 1.147
Likelihood ratio test	0.00	0.94	0.87
Males only			
3–<15 years			
ERR/10 mSv	0.280	0.369	0.437
90% CI	0.021, 0.728	0.003, 1.046	<0, 1.598
Likelihood ratio test	3.34	2.78	1.74
15–<30 years			
ERR/10 mSv	0.012	0.009	0.013
90% CI	<0, 0.109	<0, 0.167	<0, 0.364
Likelihood ratio test	0.07	0.02	0.01
≥30 years			
ERR/10 mSv	−0.003	0.104	0.211
90% CI	<0, 0.151	<0, 0.458	<0, 1.192
Likelihood ratio test	0.00	0.98	0.86

\* CLL, chronic lymphocytic leukemia; ERR, excess relative rate; CI, confidence interval.

**TABLE 4. Observed deaths of workers and estimated rate ratios by category of cumulative dose under a 3-year exposure lag assumption, Savannah River Site, South Carolina, 1950–2002**

Cause of death	Dose category (mSv)								
	0	>0–<5	5–<10	10–<20	20–<40	40–<80	80–<160	160–<320	≥320
<b>Leukemia</b>									
Observed no. of deaths	5	26	9	8	8	9	13	4	2
Rate ratio	1	1.39	1.39	1.55	1.74	2.08	3.49	1.34	4.91
<b>Leukemia excluding CLL*</b>									
Observed no. of deaths	4	19	7	6	4	5	11	4	2
Rate ratio	1	1.25	1.38	1.59	1.10	1.59	4.03	1.87	6.61
<b>Myeloid leukemia</b>									
Observed no. of deaths	4	11	3	5	3	4	6	2	2
Rate ratio	1	0.62	0.49	1.05	0.67	1.15	2.21	1.06	8.09
Mean dose (mSv)	0	1.9	7.2	14.3	28.9	56.7	115.2	219.4	360.2

\* CLL, chronic lymphocytic leukemia.

penultimate category (for which the estimated rate ratio was 1.34). In analyses of leukemia excluding CLL, there was less evidence of a monotonic trend in estimated rate ratios across dose categories; however, the estimated rate ratios for leukemia excluding CLL for the highest three dose categories were substantially larger than the values derived from analyses that included CLL. In analyses of myeloid leukemia, rate ratios were less than unity for the categories >0–<5, 5–<10, 10–<20, and 20–<40 mSv but were greater than unity for the higher dose groups.

The results in table 4 suggest a substantial increase in observed relative rates with increasing dose; we contrasted the goodness-of-model fit of an exponential rate model to the fit of the additive ERR model. For analyses of the association between cumulative dose under a 3-year lag and each category of cause of death, we found that the exponential rate model fitted the data slightly worse than the additive ERR model; for example, for analyses of leukemia excluding CLL, the residual model deviance under the exponential rate model was 732.81, whereas, under the additive ERR model, the residual deviance was 731.84.

## DISCUSSION

We observed positive associations between leukemia mortality and ionizing radiation doses from external sources and internal tritium depositions. The association between leukemia excluding CLL and cumulative radiation dose under a 3-year lag (ERR/10 mSv = 0.077) was larger than, but not incompatible with, the risk estimate (under a 2-year lag) for non-CLL leukemia in the 15-country study (ERR/10 mSv = 0.019, 95 percent CI: <0, 0.085) and analyses of mortality among A-bomb survivors (ERR/10 mSv = 0.032, 95 percent CI: 0.016, 0.057) (1). There is no overlap between the workers included in this analysis and the workers included in the 15-country study.

Via exposure time windows we observed that the ERR estimate for leukemia was 0.265 per 10 mSv for exposures accrued 3–<15 years prior, 0.011 per 10 mSv for exposures accrued 15–<30 years prior, and essentially null for exposures accrued ≥30 years prior. Such a temporal pattern of diminishing radiation dose–leukemia mortality associations with time since exposure differs from the pattern observed in the 15-country study but is consistent with observations derived from some studies of leukemia risk following acute exposure to ionizing radiation, including patients who received radiotherapy for ankylosing spondylitis (14). Among survivors of the atomic bombings of Hiroshima and Nagasaki, Japan, leukemia mortality is positively associated with ionizing radiation dose, with the preferred model allowing for diminishing effect of irradiation on leukemia risk with increasing time since exposure (2).

Although the 15-country study includes more leukemia cases than our study of Savannah River Site workers, an important consideration is the distribution of cases with respect to cumulative dose. The average dose accrued by workers in the 15-country study (19.4 mSv) is less than half the average dose accrued by males employed at the Savannah River Site. Crucially, this study of Savannah River Site workers and the 15-country study include the same number of non-CLL leukemia deaths among workers who accrued a ≥50-mSv dose (19 deaths), and this study includes more non-CLL leukemia deaths among workers who accrued ≥100 mSv than the 15-country study does (the latter includes 10 deaths in the ≥100-mSv range, whereas this study includes 13 deaths in that range) (15).

At the Savannah River Site, film badge dosimeters were exchanged on a weekly schedule until October 1957, on a biweekly schedule from October 1957 to 1964, on a 4-week cycle in 1965, and on a monthly schedule beginning in 1966 (6). Thermoluminescent dosimeters were exchanged on a quarterly cycle for personnel judged to have low-exposure potential and on a monthly cycle for other employees.

Frequent reading of dosimeters could lead to cumulative dose underestimation if dosimeters were not sufficiently exposed to reach a minimum detectable dose. However, analyses based on simulations and dose estimation procedures suggest that the impact on estimates of radiation dose-response trends of this source of exposure measurement error is modest (16–18). Recent work on radiation dosimetry for occupational cohort studies suggests that the errors that may be most important for dose estimates are those that result from the fact that dosimeters used in the earliest years of the nuclear era were limited in their ability to respond accurately for some energies and geometries of radiation exposures (19, 20). Biases resulting from these limitations may differ between facilities with different exposure conditions and will tend to be greater in analyses that include larger numbers of workers employed in the earliest year of the nuclear era. The Savannah River Site, however, started operations in the 1950s and therefore began operations in a period that benefited from experience with radiation protection and the advances in monitoring practices developed during the first decade of the Manhattan Project (17).

For nuclear worker studies of associations between radiation and leukemia mortality, the potential for confounding by nonradiologic leukemogens, such as benzene, must be considered as well. Potential confounding by benzene exposure was not assessed in the 15-country study because detailed assessments of such exposures for all facilities included in the collaborative study were not possible, although assessments for some cohorts included in the study noted a potential for occupational benzene exposures (21). In contrast, in a study that focuses on a single cohort, there is substantial opportunity for detailed evaluation of historical information on process activities and potential for significant occupational exposures to hazards other than ionizing radiation. Several assessments of nonradiologic exposures have been conducted for workers employed at the Savannah River Site indicating that benzene exposure was not a significant hazard at the site. For this study, we reviewed monthly industrial hygiene reports, two prior assessments of chemical and physical hazards (22, 23), and hazard assessments conducted as part of the Savannah River Site building database (24) to assess the potential for confounding by non-radiologic hazards that are known leukemogens. These documents show little evidence of exposure to established leukemogens other than ionizing radiation. For example, reviews of industrial hygiene reports spanning the period 1952–1986 provide little indication of benzene exposure potential. For more recent years, computerized records of industrial hygiene monitoring at the Savannah River Site were reviewed; the only monitoring for benzene exposure that occurred was limited to the laboratory areas where benzene was used in small (reagent) quantities.

Aside from the external exposures to ionizing radiation and internal depositions of tritium (which were quantified as the exposure of interest in these analyses), plutonium-239 is the primary radiologic hazard at the Savannah River Site. Plutonium delivers alpha radiation to the lung, liver, and bone surface; a very small proportion of the delivered dose is to the hematopoietic red bone marrow. While annual dose estimates for intakes of plutonium and other radionuclides

have not been computerized for all intakes over this study period, dose estimates have been derived for some leukemia cases at the Savannah River Site. These analyses suggest that plutonium contributes only about 3 percent of the total biologically equivalent dose to the red bone marrow, with the remainder due to gamma radiation and tritium (17, 25, 26). Without direct estimates of doses from all internal depositions, however, the joint effects of these exposures cannot be evaluated.

Our prior work suggests that information on cigarette smoking is incomplete in the available records from the site's medical division and is difficult to evaluate for workers prior to the middle 1960s and for all workers after termination of employment (27). However, this limitation is minor in the context of these analyses of leukemia mortality, since, given the small magnitude of association between smoking and leukemia mortality, high levels of correlation between occupational radiation exposure and smoking would be necessary to account for even modest dose-response trends for leukemia (28, 29).

Although considerations about heterogeneity in radiation dose-response analyses for different subtypes of leukemia are of interest, because of small numbers we did not conduct subtype-specific dose-response analyses. A thorough consideration of the topic would include evaluations of heterogeneity by disease subtype in the temporal pattern of radiation dose–mortality associations (30); such analyses demand relatively large numbers of cases.

In addition to the cohorts of nuclear workers aggregated for analyses in the 15-country study (1), there are several other cohorts of US nuclear workers in which associations between occupational exposure to ionizing radiation and leukemia have been examined. Two studies that included relatively large numbers of leukemias are those by Yiin et al. (31) on radiation dose–leukemia mortality association among 13,468 radiation-monitored workers employed at the Portsmouth Naval Shipyard (Maine) and by Schubauer-Berigan et al. (32) on leukemia among workers at five US nuclear facilities. Both studies are consistent with a positive association between low-level occupational exposure to ionizing radiation and non-CLL leukemia mortality characterized by a relatively short empirical induction period.

This study provides evidence of positive associations between radiation dose and leukemia mortality among workers at the Savannah River Site. The temporal patterns of association appear consistent with the temporal patterns in studies of populations exposed at higher dose rates. Associations appeared stronger for leukemia excluding CLL than for all leukemias and were of the largest magnitude for the myeloid forms of leukemia. We found relatively little evidence to support hypotheses of potential confounding by known nonradiologic leukemogens. The findings illustrate the importance of continued follow-up and analyses of these historical US Department of Energy cohorts because the evidence obtained from these studies continues to grow as the cohorts are followed over time. Persistence of dose-response associations at magnitudes observed in this analysis would be inconsistent with previous arguments that chronic low-level doses of ionizing radiation are less leukemogenic than acute exposures to the same doses.

## ACKNOWLEDGMENTS

This project was supported by grant R01 OH007871 from the National Institute for Occupational Safety and Health of the Centers for Disease Control and Prevention.

The authors thank Victor Rhodes and Steve Hutton for data management and computer programming assistance. For their invaluable assistance in determining vital status and causes of death, the authors also thank Donna Cragle, Phil Wallace, and Betsy Ellis, the Oak Ridge Associated Universities; Carolyn Watkins, Medical Coding and Consultation; Robert Bilgrad, the National Death Index; Patricia McFadden, the Social Security Administration; and the Vital Records Registrars and their staff from almost all 50 United States.

Conflict of interest: none declared.

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**APPENDIX TABLE 1. Observed deaths of workers and estimated rate ratios by category of cumulative dose accrued in the period 3–<15 years prior to case occurrence, Savannah River Site, South Carolina, 1950–2002**

Cause of death	Dose category (mSv)						
	0	>0–<5	5–<10	10–<20	20–<40	40–<80	≥80
<b>Leukemia</b>							
Observed no. of deaths	39	20	2	3	4	9	2
Rate ratio	1	1.36	0.94	1.55	2.05	5.50	1.86
<b>Leukemia excluding CLL*</b>							
Observed no. of deaths	29	14	1	2	3	8	1
Rate ratio	1	1.32	0.64	1.47	2.26	7.12	1.22
<b>Myeloid leukemia</b>							
Observed no. of deaths	13	9	1	1	2	5	1
Rate ratio	1	2.17	1.57	1.83	3.85	10.88	2.55

\* CLL, chronic lymphocytic leukemia.