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Mortality among Radiation Workers at Rocketdyne (Atomics International), 1948–1999

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A retrospective cohort mortality study was conducted of workers engaged in nuclear technology development and employed for at least 6 months at Rocketdyne (Atomics International) facilities in California, 1948–1999. Lifetime occupational doses were derived from company records and linkages with national dosimetry data sets. International Commission on Radiation Protection (ICRP) biokinetic models were used to estimate radiation doses to 16 organs or tissues after the intake of radionuclides. Standardized mortality ratios (SMRs) compared the observed numbers of deaths with those expected in the general population of California. Cox proportional hazards models were used to evaluate dose–response trends over categories of cumulative radiation dose, combining external and internal organ-specific doses. There were 5,801 radiation workers, including 2,232 monitored for radionuclide intakes. The mean dose from external radiation was 13.5 mSv (maximum 1 Sv); the mean lung dose from external and internal radiation combined was 19.0 mSv (maximum 3.6 Sv). Vital status was determined for 97.6% of the workers of whom 25.3% (n = 1,468) had died. The average period of observation was 27.9 years. All cancers taken together (SMR 0.93; 95% CI 0.84–1.02) and all leukemia excluding chronic lymphocytic leukemia (CLL) (SMR 1.21; 95% CI 0.69–1.97) were not significantly elevated. No SMR was significantly increased for any cancer or for any other cause of death. The Cox regression analyses revealed no significant dose–response trends for any cancer. For all cancers excluding leukemia, the RR at 100 mSv was estimated as 1.00 (95% CI 0.81–1.24), and for all leukemia excluding CLL it was 1.34 (95% CI 0.73–2.45). The nonsignificant increase in leukemia (excluding CLL) was in accord with expectation from other radiation studies, but a similar nonsignificant increase in CLL (a malignancy not found to be associated with radiation) tempers a causal interpretation. Radiation exposure has not caused a detectable increase in cancer deaths in this population, but results are limited by small numbers and relatively low career doses.

INTRODUCTION

Studies of workers in the nuclear industry have the potential to provide information on radiation risk after low doses delivered over many years at a low rate. Comprehensive studies have been conducted in the United States (*1–5*), the United Kingdom (*6, 7*), Canada (*8, 9*) and Japan (*10*). Studies of Chernobyl cleanup workers have also been conducted (*11*). An international study of workers in three countries (*12*) was recently expanded to include workers in 15 countries (*13*). No consistent pattern of increased radiation risks is seen, however, perhaps due in part to the relatively low doses and limited number of workers studied; i.e., when low doses are involved, even a sample size of 100,000 can be insufficient to reveal an underlying radiation effect (*14*). One exception is the study of Mayak workers in Russia who received rather large exposures to plutonium and external γ rays (*15–21*). In light of these findings, it was somewhat unexpected that a small study of fewer than 5,000 workers at the Rocketdyne (Atomics International) facilities in California exposed to lower occupational doses than in these larger studies reported significant increased cancer risks (*22–24*). The authors acknowledged, however, that their findings would have to be replicated in other series or confirmed in a further follow-up. The current independent investigation extends the previous follow-up of the Rocketdyne (Atomics International) study by 5 years. In addition, somewhat different inclusion criteria were used to select the workers for study, and considerable effort was spent ascertaining lifetime exposure to occupational radiation and computing individual organ doses from the intake of radionuclides (*25, 26*).

Rocketdyne (Atomics International) facilities in California include the Santa Susana Field Laboratory (SSFL) and the Canoga Park and De Soto sites. Atomics International was dedicated to the research and development of nuclear energy and operated ten nuclear reactors and seven criti-

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cality facilities over the years. Nine of the ten reactors operated at power levels below 1 MW. Other radiation-related activities included fabricating nuclear fuel, disassembling and decontaminating reactor facilities, decladding spent nuclear fuel, and storing nuclear material. The radiation work at the Rocketdyne facilities did not involve any nuclear weapons activities or the production or testing of nuclear weapons components. During the years 1958 through 1983, enriched uranium and plutonium fuels were fabricated for research, space and power reactors. Rocketdyne, a rocket engine test facility, merged with Atomics International in the 1950s. The company was owned and operated by various companies including North American Aviation, Rockwell International and The Boeing Company. Rocketdyne was sold in 2005 to Pratt & Whitney. For the remainder of this report, ''Rocketdyne'' will be used to represent all corporate names under which radiation work was conducted over the past 50 years.

METHODS

The study received human subjects research approval from Vanderbilt University, The Boeing Company, and the Oak Ridge Site-Wide Institutional Review Boards.

Cohort Definition

The study cohort comprised all workers who were monitored for radiation at Rocketdyne and employed on or after January 1, 1948 for at least 6 months. The primary source to identify the radiation worker cohort was the files in the Radiation Health and Safety Department, which included records of all workers ever monitored for radiation at Rocketdyne. Inclusion in the radiation cohort required evidence of actual radiation monitoring and confirmation of employment at Rocketdyne. There were 14,169 workers with radiation folders, but only 6,675 had actually been monitored for radiation. An administrative decision had been made to issue a radiation folder for all Atomics International employees regardless of whether they would be involved in radiation work. After 7,204 workers who were never monitored for radiation, 350 radiation workers employed for less than 6 months, and 524 workers with insufficient identifying information were excluded, 5,801 remained eligible for study as radiation workers.

A Rocketdyne worker population not monitored for radiation was identified for comparison from work history Kardex cards and computerized personnel files. Information on Kardex work history cards, copied for over 35,000 workers, included name, Social Security number, employee serial number, date of first hire, date of birth, a complete history of jobs [occupational title, occupational code, pay type (hourly/salary), department, date of job change, date of termination], and occasionally prior employment information. Similar work information was available on a computerized personnel listing available for over 26,000 workers employed on or after 1972. These overlapping sources identified 46,970 unique workers and provided the identifying information needed for vital status tracing. There were 41,169 workers (8,190 SSFL workers and 32,979 workers at the nearby Rocketdyne facilities at Canoga Park and De Soto) who were not monitored for radiation and who were employed for at least 6 months on or after January 1, 1948.

Vital Status Determination

Vital status as of December 31, 1999 was sought for all workers. Mortality was determined from the California death tapes (1960–1999), the California death index (1940–1960), the National Death Index (1979–1999), Pension Benefit Information (PBI) files, the Social Security Master File, the Centers for Medicare and Medicaid Services (CMS) beneficiary files (formerly the Health Care Financing Administration), employment work history cards, pension records and retirement records. Cause of death, coded according to the International Classification of Diseases (ICD) in use at the time of death, was obtained from the California death tape for those dying in California after 1959 and from the National Death Index for non-California residents dying after 1978. For all other deaths, death certificates were sought from company sources or state vital statistics departments and then coded by a trained nosologist for the underlying cause of death according to the ICD codes in use at the time of death. A cause of death was obtained for all but 25 (1.7%) of the 1,468 radiation workers found to have died.

Sources to confirm alive status included company employment and retirement records, CMS files for study subjects over age 65, and Social Security Administration files for study subjects under age 65. The 142 (or 2.4%) cohort members not confirmed as alive by these sources or not found to have died were assumed to be alive up until their date of last employment at Rocketdyne. For all 46,970 Rocketdyne workers studied, 368 (or 0.8%) were lost to follow-up, and death certificates were obtained for all but 280 (or 2.5%) of the 11,118 workers who had died.

Assessment of Exposures

The approach to obtaining career doses for the workforce has been described in detail (*25*). Briefly, all 14,169 folders in the Radiation Health and Safety Department were scanned into computer-searchable image files. All individual folders were evaluated as to whether the worker was actually monitored for radiation, and each monitored worker was then classified as to whether he or she was monitored for external radiation, internal radiation or both. External radiation was abstracted on a year-by-year basis, and bioassay data on radionuclide intakes were processed so that yearly doses for 16 organs or tissues could be estimated using current International Commission on Radiation Protection (ICRP) biokinetic models. For workers with intakes of uranium aluminide, the ICRP respiratory model was modified to account for delayed dissolution of inhaled material in the respiratory tract (*26*). Annual radiation doses received before and after employment at Rocketdyne were also obtained from various national databases including the Department of Energy, the Nuclear Regulatory Commission, Landauer, Inc., and U.S. military services. These data were then combined and organ doses estimated for each worker taking into account external (both photon and neutron) and internal radiation exposures. All analyses are based on cumulative occupational doses received at all places of employment unless otherwise stated.

Analytical Methods

External comparisons contrasted observed number of deaths with that expected based on mortality rates in the general population of California. Intra-cohort dose–response comparisons were made using Cox proportional hazards models (*27, 28*), which contrasted rates of disease over categories of exposure to both external and internal radiation, controlling for potential confounding factors.

1. External (SMR) analyses

Observed numbers of deaths from cancers and all other diseases were counted by race, gender, age and calendar year for workers overall and for subgroups defined by time since first exposure, duration of employment, and exposure to external and internal radiation. Expected numbers of deaths were computed based on race-, age-, calendar year- and gender-specific mortality rates in the general population of California. For the 13% of workers with unknown race, a weighted approximation based on the proportions of race for the 87% of workers with known race was used to compute expected numbers (*29*).

Person-years of follow-up began 6 months after the date of first radiation monitoring or July 1, 1948 depending on which came later. Person-

TABLE 1
Demographic and Occupational Characteristics of Rocketdyne Workers Who Were Monitored for External Radiation and Internal Radiation, 1948–1999

Characteristic	Any external		Any internal		Total	
	n	Percent	*n*	Percent	*n*	Percent
Gender						
Male	5,281	92.0	2,149	96.3	5,335	92.0
Female	462	8.0	83	3.7	466	8.0
Race						
White	4,651	81.0	1,754	78.6	4,695	80.9
Non-white	335	5.8	130	5.8	340	5.8
Missing	757	13.2	348	15.6	766	13.2
Pay type						
Hourly	3,243	56.5	1,398	62.6	3,285	56.6
Salary	2,500	43.5	834	37.4	2,516	43.4
Monitored for radiation						
External radiation only	3,569	62.1	0	0.0	3,569	61.5
External and internal radiation	2,174	37.9	2,174	97.4	2,174	37.5
Internal radiation only	0	0.0	58	2.6	58	1.0
Radiation monitoring elsewhere						
Before Rocketdyne	930	16.2	572	25.6	932	16.1
After Rocketdyne	1,219	21.2	499	22.4	1,224	21.1
Year of birth						
<1920	930	16.2	348	15.6	937	16.2
1920–1929	1,657	28.9	582	26.1	1,670	28.8
1930–1939	1,689	29.4	692	31.0	1,701	29.3
1940–1949	755	13.1	384	17.2	769	13.3
1950–1959	524	9.1	192	8.6	534	9.2
≥1960	188	3.3	34	1.5	190	3.3
Year of hire						
<1948	98	1.7	21	0.9	98	1.7
1948–1959	2,461	42.9	850	38.1	2,471	42.6
1960–1969	1,934	33.7	935	41.9	1,963	33.8
1970–1979	598	10.4	307	13.8	607	10.5
1980–1989	586	10.2	110	4.9	595	10.3
≥1990	66	1.1	9	0.4	67	1.2
Year of termination						
<1960	319	5.6	10	0.4	319	5.5
1960–1969	2,345	40.8	978	43.8	2,370	40.9
1970–1979	917	16.0	442	19.8	924	15.9
1980–1989	830	14.5	373	16.7	844	14.5
1990–1999	809	14.1	249	11.2	817	14.1
Active (12/31/1999)	523	9.1	180	8.1	527	9.1
Duration of employment (years)						
0.5–0.9	211	3.7	87	3.9	215	3.7
1–4	1,708	29.7	690	30.9	1,730	29.8
5–9	1,194	20.8	509	22.8	1,205	20.8
10–14	932	16.2	365	16.4	939	16.2
15–19	575	10.0	213	9.5	579	10.0
≥20	741	12.9	257	11.5	748	12.9
Missing	382	6.7	111	5.0	385	6.6
Years of follow-up						
<1	94	1.6	9	0.4	95	1.6
1–4	191	3.3	17	0.8	191	3.3
5–9	347	6.0	67	3.0	349	6.0
10–19	873	15.2	260	11.6	886	15.3
20–29	1,062	18.5	532	23.8	1,075	18.5
30–39	2,336	40.7	1,036	46.4	2,360	40.7
40–49	833	14.5	309	13.8	837	14.4
≥50	7	0.1	2	0.1	8	0.1

TABLE 1
Continued

Characteristic	Any external		Any internal		Total	
	n	Percent	*n*	Percent	*n*	Percent
Vital status as of 12/31/1999						
Alive	4,153	72.3	1,626	72.8	4,191	72.2
Dead	1,449	25.2	599	26.8	1,468	25.3
Lost to follow-up	141	2.5	7	0.3	142	2.4
Total	5,743		2,232		5,801	

years stopped at the date of death, December 31, 1999, age 95 or date lost to follow-up, whichever came first. Ratios of observed to expected deaths (or standardized mortality ratios, SMRs) were computed and 95% confidence intervals (95% CIs) calculated (*29*). To account for the favorable mortality experience primarily with respect to cardiovascular and other diseases seen among newly hired workers, SMR analyses were also conducted excluding the first 10 years of follow-up after date of hire (data not shown). Similarly, in some analyses, exposures were lagged 10 years for solid cancers and 2 years for leukemia; i.e., exposures occurring in these intervals prior to end of follow-up were excluded. Observed and expected numbers of deaths were also distributed over categories of external radiation dose and trend analyses were conducted following the methods of Breslow and colleagues (*30–32*). Person-years of observation were distributed to increasingly higher dose categories over time as radiation doses accrued for individual workers; i.e., person-years were not all assigned to the final cumulative dose category (*29*). These SMR analyses based on external radiation doses were conducted for all causes of death to provide a focus for the more robust intra-cohort analyses described below that incorporate the internal radiation doses to specific organs and apply the more powerful Cox regression methods.

2. Intra-cohort dose–response analyses

Intra-cohort (or internal) comparisons would be expected to minimize any biases that might exist when external comparisons with a general population are made. Accordingly, intra-cohort dose–response comparisons were made to assess risk within the cohort over categories of radiation dose to specific organs. Relative risks were estimated by Cox proportional hazards modeling techniques with trend tests conducted to learn whether there were significant increases in risk with increasing levels of radiation dose (*27*). The nonexposed referent category consisted of Rocketdyne workers who were not monitored for radiation. Year of birth, year of hire, gender, pay type (hourly/salary), and duration of employment were included in all models. Pay type was considered a surrogate measure of socio-economic status. Because of their hands-on experience with large quantities of engine fuels, oxidizers and solvents, rocket test stand mechanics were considered a unique group with the highest potential exposure to toxic substances. Overall, there were 1,651 rocket test stand mechanics, of whom 182 had also been monitored for radiation at some time during their career. Adjustment for work as a test stand mechanic was made in the analyses.

Radiation workers entered the risk set at their first date of radiation monitoring at Rocketdyne plus 6 months. Workers not monitored for radiation entered the risk set at their first date of hire at Rocketdyne plus 6 months. Radiation exposure category was treated as a time-dependent covariate, allowing workers to be assigned to increasingly higher dose categories over time as their individual radiation doses accrued. Exposure categories were selected based on *a priori* cut points where possible (*25*). The parameter estimates and standard errors for the exposure categories in the Cox models were used to obtain risk (or hazard) ratios and confidence intervals for death due to the cause under investigation compared to those in the referent group. To allow for a possible latent period between an exposure and any effect consequent to it, doses were lagged, i.e., excluded if they occurred during some assumed latent interval prior to the event of interest. For most intra-cohort dose–response analyses, doses were lagged 10 years for solid cancers and 2 years for leukemia.

Trend tests were conducted by treating the radiation dose as a single, time-dependent continuous measure, and one-sided *P* values are presented unless otherwise stated. Relative risks at 100 mSv were computed for all cancers excluding leukemia, all leukemia excluding chronic lymphocytic leukemia (CLL), and lung cancer.

Analyses were also conducted to assess the impact of the choice of analytical strategy on the estimates or radiation risk. The ''standard'' Cox proportional hazards model included adjustments for year of birth, year of hire, gender, pay type (hourly/salary), duration of employment, and work as a rocket test stand mechanic. Workers who held hourly jobs for at least 20% of their career were classified as hourly workers. Comparisons were made with all Rocketdyne workers who were not monitored for radiation as the referent group, but other referent groups were evaluated to learn whether results would be affected. Changes in the RR estimates at 100 mSv were evaluated for a range of alternative assumptions. Analyses were also conducted to examine the possible modifying effects of age at exposure, attained age, and time since exposure, and tests of homogeneity were carried out. Finally, doses were lagged at different intervals (5, 10, 15 and 20 years), and analyses were conducted to compare different choices of lag.

RESULTS

Table 1 presents the demographic and occupational characteristics of the 5,801 radiation workers. The majority of workers were male (92.0%), white (80.9%), hourly (56.6%), born prior to 1940 (74.3%), hired prior to 1970 (78.1%), terminated employment prior to 1980 (62.3%), employed for more than 5 years (59.9%), followed for more than 30 years (55.2%), and alive as of December 31, 1999 (72.2%). Overall, 61.5% of the workers were monitored only for external radiation, 37.5% were monitored for both external and internal radiation, and 1% only for internal radiation. Nearly 32% (or 1,833) of those monitored for radiation at Rocketdyne had been employed elsewhere where they had been monitored for radiation exposures. Some workers were monitored for radiation both before and after employment at Rocketdyne. Over 10% (or 604) of the monitored workers received more exposure elsewhere than they had received at Rocketdyne (*25*). Among workers not monitored for radiation at Rocketdyne, 3.6% (or 1,478) had been monitored elsewhere (mean dose, 2.6 mSv). Among the 2,232 (or 38.5%) workers monitored for internal radiation, most (1,940 or 86.9%) had negligible intakes; i.e., bioassay measurements indicated that their committed equivalent dose to any tissue was well below 10 mSv (*25*)

TABLE 2
Observed (Obs) Numbers of Deaths and Standardized Mortality Ratios (SMRs)[a] for Rocketdyne Workers Monitored for Radiation by Type of Radiation Monitoring (External, Internal)

Type of monitoring	Any external radiation			Any internal radiation[b]			Total[a]		
No. of workers	5,743			2,232			5,801		
Person-years	159,971			67,773			161,605		
Cause of death (ICD9)	Obs	SMR[a]	95% CI	Obs	SMR[a]	95% CI	Obs	SMR[a]	95% CI
All causes of death (001–999)	1,449	0.78	0.74–0.82	599	0.81	0.75–0.88	1,468	0.79	0.75–0.83
All malignant neoplasms (140–208)	447	0.89	0.81–0.98	203	1.04	0.90–1.19	456	0.90	0.82–0.99
Buccal cavity and pharynx (140–149)	8	0.62	0.27–1.23	4	0.78	0.21–1.99	8	0.62	0.27–1.22
Esophagus (150)	10	0.72	0.35–1.33	7	1.27	0.51–2.61	12	0.86	0.44–1.50
Stomach (151)	21	1.18	0.73–1.81	12	1.70	0.88–2.97	21	1.17	0.73–1.79
Colorectal (153–154)	56	1.13	0.85–1.47	26	1.35	0.89–1.97	56	1.13	0.85–1.47
Biliary passages and liver (155, 156)	5	0.37	0.12–0.87	1	0.19	0.01–1.04	5	0.37	0.12–0.86
Pancreas (157)	21	0.80	0.50–1.23	9	0.88	0.40–1.67	21	0.80	0.49–1.22
Larynx (161)	9	1.64	0.75–3.11	6	2.74	1.01–5.96	9	1.63	0.74–3.09
Bronchus, trachea and lung (162)	148	0.88	0.75–1.04	69	1.05	0.81–1.32	151	0.89	0.76–1.05
Breast (174, 175)	5	0.89	0.29–2.07	1	0.81	0.02–4.52	5	0.88	0.29–2.05
All uterine (females only) (179–182)	0	(1.2)	0.00–3.02	0	(0.2)	0.00–15.20	0	(1.2)	0.00–2.99
Cervix uteri (180)	0	(0.6)	0.00–5.84	0	(0.1)	0.00–28.52	0	(0.6)	0.00–5.78
Other female genital organs (183–184)	0	(1.7)	0.00–2.22	0	(0.3)	0.00–11.48	0	(1.7)	0.00–2.20
Prostate (males only) (185)	37	0.94	0.66–1.30	17	1.11	0.65–1.78	37	0.93	0.66–1.29
Testes and other male genital organs (186, 187)	1	0.69	0.02–3.86	1	1.58	0.04–8.79	1	0.69	0.02–3.82
Kidney (189.0–189.2)	11	0.87	0.43–1.55	7	1.39	0.56–2.86	12	0.94	0.49–1.64
Bladder and other urinary (188, 189.3–189.9)	8	0.66	0.28–1.30	3	0.64	0.13–1.86	8	0.65	0.28–1.29
Melanoma of skin (172)	7	0.72	0.29–1.49	4	1.02	0.28–2.60	8	0.82	0.35–1.62
Brain and CNS (191–192)	15	1.02	0.57–1.68	5	0.84	0.27–1.96	17	1.15	0.67–1.83
Thyroid and other endocrine glands (193–194)	0	(1.6)	0.00–2.30	0	(0.6)	0.00–5.84	0	(1.6)	0.00–2.29
Bone (170)	0	(1.0)	0.00–3.55	0	(0.4)	0.00–8.73	0	(1.0)	0.00–3.52
All lymphatic, hematopoietic tissue (200–208)	51	1.03	0.77–1.36	21	1.07	0.66–1.64	51	1.03	0.76–1.35
Hodgkins lymphoma (201)	5	2.00	0.65–4.68	2	1.92	0.23–6.93	5	1.99	0.65–4.63
Non-Hodgkins lymphoma (200, 202)	19	0.98	0.59–1.54	8	1.05	0.45–2.06	19	0.98	0.59–1.52
Multiple myeloma (203)	2	0.24	0.03–0.86	1	0.31	0.01–1.70	2	0.24	0.03–0.86
Leukemia and aleukemia (204–208)	25	1.34	0.87–1.98	10	1.35	0.65–2.49	25	1.33	0.86–1.97
Chronic lymphocytic leukemia (204.1)	7	2.06	0.83–4.24	4	3.03	0.83–7.76	7	2.04	0.82–4.21
Leukemia other than CLL	18	1.17	0.70–1.85	6	0.98	0.36–2.13	18	1.16	0.69–1.84
Pleura and peritonium (158.8, 158.9, 163) and mesothelioma (ICD 10 C45)	1	1.01	0.03–5.65	0	(0.4)	0.00–9.55	1	1.01	0.03–5.61
Smoking-related cancers (140–150, 161–162, 157, 188, 189)	215	0.86	0.75–0.98	105	1.06	0.87–1.29	221	0.87	0.76–1.00
AIDS (042–044, 795.8)	1	0.06	0.00–0.33	0	(7.8)	0.00–0.47	1	0.06	0.00–0.33
Diabetes (250)	18	0.57	0.34–0.90	8	0.64	0.28–1.26	18	0.56	0.33–0.89
Mental and behavioral disorders (290–319)	13	0.75	0.40–1.28	5	0.70	0.23–1.64	13	0.74	0.39–1.27
Diseases of the nervous system and sense organs (320–389)	30	0.97	0.65–1.38	9	0.75	0.34–1.42	30	0.96	0.65–1.37
Cerebrovascular disease (430–438)	66	0.71	0.55–0.90	32	0.89	0.61–1.26	67	0.71	0.55–0.91
All heart disease (390–398, 404, 410–429)	494	0.77	0.71–0.85	191	0.76	0.66–0.88	499	0.78	0.71–0.85
Non-malignant respiratory disease, excluding influenza and pneumonia (460–479, 488–519)	67	0.66	0.51–0.84	32	0.82	0.56–1.16	68	0.67	0.52–0.84
Emphysema (492)	17	0.75	0.44–1.20	9	1.03	0.47–1.95	17	0.75	0.43–1.19
Cirrhosis of liver (571)	37	0.52	0.37–0.72	15	0.51	0.29–0.85	38	0.53	0.38–0.73
Nephritis and nephrosis (580-589)	12	1.19	0.62–2.08	4	1.01	0.28–2.59	12	1.18	0.61–2.06
All external causes of death (800–999)	106	0.67	0.55–0.81	37	0.53	0.38–0.74	106	0.67	0.55–0.81
Accidents (850–949)	60	0.66	0.50–0.84	20	0.50	0.30–0.77	60	0.65	0.49–0.83
Suicides (950–959)	31	0.67	0.46–0.96	9	0.46	0.21–0.87	31	0.67	0.45–0.95
Unknown causes of death	25			8			25		

[a] Expected number of deaths is shown in parentheses when the observed number is zero.
[b] All but 58 workers monitored for internal uptake of radionuclides were also monitored for external radiation.

and thus was very small compared to the cumulative dose received from natural background radiation.

Table 2 presents the standardized mortality ratios for 44 causes of death by type of radiation monitoring, comparing the observed numbers of deaths with those expected in the general population of California. The Rocketdyne radiation workers had a lower risk of dying from all causes (SMR 0.79; 1,468 observed compared to 1,870 expected) and from all cancers (SMR 0.90; 456 observed compared to 505 expected) than the general California population.

Overall, there were no significantly elevated SMRs for any site or for all cancers combined (SMR 0.90; 95% CI 0.8–1.0). Lung cancer was not increased (SMR 0.89; 95% CI 0.76–1.05), nor were other sites of interest, i.e., cancers of the liver (SMR 0.37, $n = 5$), bone (SMR 0.0), esophagus (SMR 0.85; $n = 12$) and kidney (SMR 0.94, $n = 12$). All leukemias combined were slightly elevated, but not significantly (SMR 1.33, $n = 25$), and the SMR for chronic lymphocytic leukemia (CLL) was higher (SMR 2.04) than the SMR for the other leukemias (SMR 1.16). Significant deficits were seen for heart disease, cerebrovascular disease, cirrhosis of the liver and all external causes of death. Only one death due to mesothelioma or cancer of the pleura was observed compared to 1.0 expected.

SMRs for the subset of 2,232 workers who were monitored for internal radiation were slightly higher than for the 5,743 workers monitored for external radiation, but not significantly. Practically all the workers monitored for internal radiation (97.5%) were also monitored for external exposures. Most workers monitored for internal radiation had insignificant intakes of radionuclides based on bioassay measurements and other internal monitoring data; i.e., the projected lifetime doses were small compared with doses normally received from natural background sources of radiation, and only 292 workers had levels sufficiently high to warrant detailed organ dose determination (*25*). The criterion for selecting workers for assessment of organ doses from internally deposited radionuclides was that projected lifetime equivalent doses from all intakes combined were at least 10 mSv to any tissue (*25*). Among workers monitored for internal radiation, an increase of cancer of the larynx was of borderline significance (SMR 2.74; 95% CI 1.0–6.0; $n = 6$) as was a decrease of cancer of the liver (SMR 0.19, 95% CI 0.0–1.0; $n = 1$). Cancers of the kidney (SMR 1.39; $n = 7$), bladder (SMR 0.64; $n = 3$), bone (SMR = 0.0), pancreas (SMR=0.88; $n = 9$) and prostate (SMR 1.11; $n = 17$) were not significantly increased or decreased. Workers monitored for internal radiation had higher SMRs than workers monitored for external radiation for lung cancer (SMR 1.05 compared to 0.88) and for all smoking-related sites combined (SMR 1.06 compared to 0.86), but these differences were not significant.

To account for the healthy worker effect and to exclude follow-up years for which adverse effects from occupational exposure would be unlikely to occur, analyses were also conducted that excluded the first 10 years of follow-up except for leukemia, where the first 2 years are excluded (data not shown). Exclusion of these early years of observation did not change the results appreciably; i.e., the Rocketdyne workforce still was seen to have a lower risk of death than the general population of California for all causes (SMR 0.80; 95% CI 0.76–0.85) and for all cancers taken together (SMR 0.93; 95% CI 0.84–1.02). Because most of the workforce had terminated employment 20 years prior to the close of study, the so-called healthy worker effect related to continued employment would be expected to be diminished for cancers as observed.

Table 3 presents observed numbers of deaths with those expected in the general population of California for 35 cause of death categories for all workers ever monitored for radiation at Rocketdyne. The seven categories of external radiation dose included exposures received before, during and after employment at Rocketdyne. Internal radiation doses are not included. Doses are lagged 10 years for solid cancers and 2 years for leukemia. Among the 281 workers who accumulated more than 50 mSv, 29 cancer deaths occurred and 30 were expected. Few workers, only 63, had cumulative external doses greater than 200 mSv and only six cancer deaths (compared to 5.3 expected) occurred among these workers.

The Poisson trend *P* values (*31*) in Table 3 are two-sided since many of the diseases are not considered radiogenic, e.g. diabetes or suicide. The Poisson trend statistic for indirectly standardized rates can be regarded as a rough approximation to the more robust methods used for Table 4, i.e., Cox time-dependent regression analyses incorporating internal radiation dose to specific organs. Nonetheless, the trend tests for Table 3 provide indications of the variation in causes of death over dose categories and direct attention to sites for which additional attention is warranted in Table 4.

Trends in the observed to expected numbers of cancer deaths over categories of external radiation dose were evaluated for 20 individual cancers, of which 10 were positive and 10 were negative, a distribution consistent with chance (Table 3). A significant negative association with external dose was seen for all causes of death combined, which stemmed mainly from significant negative trends for heart disease and non-malignant respiratory disease. The trends for all cancers combined and for lung cancer were not significant. A trend of borderline significance ($P = 0.04$) was seen for stomach cancer that appeared to be driven by a low SMR among the ''not monitored'' group. A significant trend in all leukemias combined was due primarily to a significant trend in CLL, a site not considered inducible by radiation (*37*). The trend for the non-CLL leukemias known to be associated with radiation was not significant ($P = 0.18$).

Table 4 presents intra-cohort dose–response analyses for 13 cancer categories and nonmalignant respiratory disease based on Cox proportional hazards models combining external radiation dose with organ-specific internal radiation dose. As described in detail elsewhere (*25*), the organ doses

TABLE 3
Observed (Obs) and Expected[a] (Exp) Numbers of Deaths for Workers Monitored for Radiation over Categories of External Radiation Dose, Doses Lagged 10 Years for Solid Cancers and 2 Years for Leukemia

External radiation dose (mSv)	Not monitored		<5		5−	
No. of workers starting interval	41,169		5,762		1,249	
Person-years of observation	1,133,261		116,650		14,671	
Cause of death (ICD9)	Obs	Exp[a]	Obs	Exp	Obs	Exp
All causes of death (001–999)	9650	10,951.2	937	1196.5	179	219.9
All malignant neoplasms (140–208)	2733	2950	270	317.4	57	60
Buccal cavity and pharynx (140–149)	56	72.7	3	8.2	1	1.5
Esophagus (150)	61	73.6	7	8.6	2	1.7
Stomach (151)	88	101.3	11	11.4	1	2.1
Colorectal (153–154)	247	290.2	36	31.3	3	6
Biliary passages and liver (155–156)	56	76.4	4	8.4	0	1.6
Pancreas (157)	148	151.8	10	16.5	3	3.1
Larynx (161)	33	29.3	3	3.5	2	0.7
Bronchus, trachea, lung (162)	917	931.4	97	105	17	20.2
Breast (174–175)	103	114.5	5	4.7	0	0.4
Prostate (males only) (185)	192	197.4	22	23.6	7	5.3
Kidney (189.0–189.2)	74	69.9	5	8	1	1.5
Bladder and other urinary (188, 189.3–189.9)	57	66.0	7	7.5	0	1.5
Melanoma of skin (172)	47	55.4	5	6.3	2	1.1
Brain and CNS (191–192)	85	87.5	11	9.7	2	1.7
All lymphatic, hematopoietic tissue (200–208)	263	287.9	24	31.7	12	5.8
Hodgkins lymphoma (201)	18	16.2	4	1.9	0	0.2
Non-Hodgkins lymphoma (200, 202)	103	112.7	8	12.3	8	2.3
Multiple myeloma (203)	40	47.7	0	5.2	1	1
Leukemia and aleukemia (204–208)	99	108.1	12	11.3	3	2.4
Chronic lymphocytic leukemia (204.1)	18	18.7	2	2	1	0.4
Leukemia other than CLL	81	90.2	10	9.3	2	2
Pleura and peritonium (158.8, 158.9, 163) and mesothelioma (ICD 10 C45)[c]	7	5.4	0	0.6	1	0.1
Smoking-related cancers (140–150, 161–162, 157, 188, 189)	1346	1394.6	132	157.3	26	30.2
Diabetes (250)	157	189.2	11	20.2	2	3.8
Cerebrovascular disease (430–438)	486	580.1	42	59.5	12	11.7
All heart disease (390–398, 410–429)	3339	3633.1	313	406.5	57	77.5
Non-malignant respiratory disease, excluding influenza and pneumonia (460–479, 488–519)	571	587.6	42	62.9	14	12.8
Emphysema (492)	121	133.2	12	14.5	2	2.8
Cirrhosis of liver (571)	234	410.6	29	47.2	4	7.7
Nephritis and nephrosis (580-589)	58	60.2	8	6.5	3	1.2
All external causes of death (800–999)	671	1004	89	114.3	7	14.7
Accidents (850–949)	399	585.4	50	67.4	4	8.4
Suicides (950–959)	215	285.5	26	32.7	2	4.6
Unknown causes of death	255		17		1	

[a] Expected number based on California population mortality rates.

[b] *P* values are two-sided since many causes of death, e.g. diabetes, have not been associated with radiation. For some sites with sparse numbers, the *P* value was computed collapsing the dose categories. The trend test is provided to indicate the variation of observed and expected causes of death over categories of external radiation dose (*31*). The more optimal dose-response trends are found in Table 4, where internal radiation dose is included and the more powerful Cox regression analysis is used (*27*).

[c] Mesothelioma was not a codeable cause of death until 1999: ICD10 (C45). Before 1999, deaths from cancer of the pleura and peritoneum (ICD9 158.8, 158.9, 163) are used to approximate mesothelioma mortality.

from internal radionuclides were computed using ICRP biokinetic models on a year-by-year basis after intake and combined with the yearly external doses for these time-dependent analyses. These causes of cancer death were selected because of *a priori* interest as radiosensitive sites, e.g. leukemia, or if the total number of deaths was at least 20. The large nonexposed group of workers was taken as the referent category to provide statistical stability in the risk estimates and trend evaluations. These intra-cohort analyses are considered more valid than the SMR analyses presented in Table 3 because potential biases associated with general population comparisons are eliminated. Analyses were adjusted for SES (i.e. pay type), duration of employment, year of birth, year of hire, and gender.

The all-cancer (excluding leukemia) analyses were over categories of external dose, whereas the categories for the other cancers incorporated both external and internal radiation doses to specific organs (*25*). The number of workers

TABLE 3
Extended

10− 1,200 22,983		50− 281 3,821		100− 146 2,251		≥200 63 1,229		Total (monitored) 5,801 161,605		Trend test, *P* value[b] (direction)
Obs	Exp	Obs	Exp	Obs	Exp	Obs	Exp	Obs	Exp	
270	348.5	39	58.9	26	30	17	18.2	1468	1872	<0.01 (−)
100	98	9	16.1	14	8.7	6	5.3	456	505.6	0.60 (+)
3	2.5	1	0.4	0	0.2	0	0.1	8	12.9	0.78 (+)
3	2.8	0	0.5	0	0.3	0	0.2	12	14	0.90 (−)
6	3.4	2	0.6	0	0.3	1	0.2	21	17.9	0.04 (+)
14	9.7	1	1.6	2	0.8	0	0.5	56	50	0.09 (+)
1	2.7	0	0.4	0	0.2	0	0.2	5	13.5	0.13 (−)
7	5.1	1	0.8	0	0.5	0	0.3	21	26.4	0.82 (−)
4	1.1	0	0.2	0	0.1	0	0.1	9	5.5	0.19 (+)
28	33.5	0	5.4	6	3.1	3	1.9	151	169	0.36 (−)
0	0.5	0	0.1	0	0	0	0	5	5.7	0.61 (−)
6	8.3	0	1.4	2	0.7	0	0.4	37	39.7	0.73 (−)
3	2.5	1	0.4	2	0.2	0	0.1	12	12.8	0.28 (+)
1	2.4	0	0.4	0	0.2	0	0.1	8	12.3	0.22 (−)
1	1.8	0	0.3	0	0.2	0	0.1	8	9.8	0.70 (−)
2	2.7	2	0.5	0	0.3	0	0.2	17	14.9	0.67 (+)
11	9.4	1	1.6	1	0.8	2	0.5	51	49.8	0.08 (+)
0	0.3	0	0.1	0	0	1	0	5	2.5	0.31 (+)
3	3.7	0	0.6	0	0.3	0	0.2	19	19.5	0.76 (+)
1	1.7	0	0.3	0	0.1	0	0.1	2	8.4	0.22[b] (−)
7	3.9	1	0.6	1	0.3	1	0.2	25	18.8	0.01 (+)
3	0.7	0	0.1	1	0.1	0	0	7	3.4	<0.01 (+)
4	3.2	1	0.5	0	0.3	1	0.2	18	15.5	0.18 (+)
0	0.2	0	0	0	0	0	0	1	1	0.95[b] (−)
49	50	3	8.2	8	4.5	3	2.8	221	252.9	0.57 (−)
3	6.2	0	1	1	0.5	1	0.3	18	32.1	0.39 (−)
9	17.5	4	3.1	0	1.3	0	0.8	67	93.9	0.20 (−)
101	122	15	20.8	7	10.3	6	6.2	499	643.4	0.01 (−)
9	20.4	2	3.4	1	1.7	0	1.1	68	102.3	<0.01 (−)
2	4.3	0	0.7	1	0.3	0	0.2	17	22.8	0.40 (−)
1	12.7	3	2.1	1	1.2	0	0.7	38	71.7	0.39 (−)
1	1.9	0	0.3	0	0.1	0	0.1	12	10.1	0.98 (+)
8	22.9	2	3.9	0	2.2	0	1.2	106	159.2	0.10 (−)
5	13	1	2.2	0	1.2	0	0.7	60	92.8	0.16 (−)
3	7.2	0	1.2	0	0.7	0	0.4	31	46.8	0.13 (−)
5		1		0		1		25		

starting each dose interval and the associated person-years varied somewhat for each cause-of-death category because of the differing contributions of internal radiation dose to different organs (*25*). Only the numbers for the ''all cancer excluding leukemia'' category are present based on external dose because, other than for lung dose and bone marrow dose the contribution of internal radiation was not that appreciable. The variations for lung and bone marrow dose are presented in Table 4. Because of small numbers, high-dose categories had to be combined for model convergence for most sites. No analyses were conducted using effective dose—a unit used in radiation protection that, while generally related to future risk, is not appropriate for retrospective epidemiological evaluation of radiation risks to specific organs or tissue (*34*). Doses were lagged by 10 years for solid cancers and by 2 years for leukemia. All *P* values are one-sided.

There were no significant increases seen for all solid cancers taken together (Fig. 1), lung cancer or any other cancer (Table 4). Nonsignificant increasing trends were seen for kidney cancer, brain cancer, leukemia and lymphomas, and nonsignificant decreasing trends were seen for cancers of the colon and rectum, pancreas, prostate and bladder and for nonmalignant respiratory disease. Stomach cancer did not show a significant trend ($P = 0.25$), in contrast to the SMR analysis presented in Table 3. Analyses were limited due to small numbers for some cancers; e.g., only three kidney cancers occurred among workers exposed to >50 mSv ($P = 0.11$) and only one bladder cancer occurred among workers exposed to >10 mSv ($P = 0.13$). The risk

TABLE 4
Intra-cohort Dose–Response[a] and Relative Risk (RR) Computations for Selected Cancers for Workers Monitored for Radiation over Categories of Organ-Specific Radiation Doses[b] with Doses Lagged 10 Years for Solid Cancer and 2 Years for Leukemia

Cause of death (ICD9)	Dose (mSv)[b]	Not monitored	<5
All cancers, excluding leukemia	Person-years	1,133,261	116,650
	No. of workers[d]	41,169	5,762
	Observed	2,635	258
	RR	1.00	0.90
	95% CI	Ref	0.78–1.04
Stomach (151)	Observed	88	11
	RR	1.00	1.04
	95% CI	Ref	0.50–2.16
Colorectal (153–154)	Observed	247	36
	RR	1.00	1.14
	95% CI	Ref	0.76–1.70
Pancreas (157)	Observed	148	10
	RR	1.00	0.63
	95% CI	Ref	0.32–1.24
Bronchus, trachea, lung (162)	Observed	917	96
	RR	1.00	0.99
	95% CI	Ref	0.78–1.25
Prostate (males only) (185)	Observed	192	22
	RR	1.00	0.83
	95% CI	Ref	0.51–1.37
Kidney (189.0–189.2)	Observed	74	5
	RR	1.00	0.53
	95% CI	Ref	0.20–1.47
Bladder and other urinary (188, 189.3–189.5)	Observed	57	7
	RR	1.00	1.12
	95% CI	Ref	0.44–2.84
Brain and CNS (191–192)	Observed	85	11
	RR	1.00	1.21
	95% CI	Ref	0.62–2.37
All lymphatic and hematopoietic tissue (200–208)	Observed	263	24
	RR	1.00	0.85
	95% CI	Ref	0.54–1.32
All lymphoma (2000–2003)	Observed	161	12
	RR	1.00	0.69
	95% CI	Ref	0.37–1.30
Leukemia excluding CLL	Observed	80	10
	RR	1.00	1.23
	95% CI	Ref	0.62–2.45
Chronic lymphocytic leukemia (204.1)	Observed	18	2
	RR	1.00	0.90
	95% CI	Ref	0.19–4.20
Non-malignant respiratory disease, excluding influenza and pneumonia (460–479, 488–519)	Observed	792	70
	RR	1.00	0.80
	95% CI	Ref	0.61–1.05

[a] All models adjusted for year of birth, year of hire, gender, internal monitoring, pay type (hourly/salary), duration of employment, and work as a test stand mechanic.

[b] Dose categories include external radiation doses received before, during, and after employment at Rocketdyne. External radiation doses plus any internal doses from the intake of radionuclides are included for all organs except the ''all cancer excluding leukemia'' category where the cancers are distributed and analyzed over categories of external dose.

[c] *P* value for test for linear trend in the relative risk (i.e., hazard ratio) computed over categories of organ dose *(27)*. (+) denotes a positive trend, (−) denotes a negative trend. *P* values are one-sided.

[d] Number of workers starting the dose interval. Although the number of workers differed across categories of dose because of the differing contribution of internal radiation dose to different organs, only the categories of lung dose and bone marrow dose changed appreciably; i.e., for lung the numbers starting each lung dose category are 5,762, 1,229, 1,293, 412 and 102 and for leukemia excluding CLL the numbers starting each bone marrow dose category are 5,762, 1,316, 1,258, and 334.

[e] Because of small numbers, convergence over the full range of dose categories was possible only for ''all cancers, excluding leukemia''. For lung cancer, dose categories 50–199 mSv were combined; dose categories 5–49 mSv and ≥50 mSv were combined for kidney cancer and for non-malignant respiratory disease; and >5 mSv for bladder cancer. For lung cancer, the RR (95% CI) for ≥50 mSv was 0.77 (0.39–1.55).

TABLE 4
Extended

5−	10−	50−	100−	≥200	Trend test[e] *P* value (direction)
14,671	22,983	3,821	2,251	1,229	
1,249	1,200	281	146	63	0.45 (+)
54	93	8	13	5	
0.94	1.00	0.53	1.60	1.11	
0.70–1.27	0.77–1.29	0.26–1.07	0.90–2.86	0.45–2.73	
1	6	3[e]			0.25 (+)
0.40	1.42	2.33	—	—	
0.05–3.21	0.46–4.43	0.55–9.84	—	—	
3	14	3[e]			0.24 (−)
0.43	1.14	0.76	—	—	
0.12–1.38	0.57–2.29	0.22–2.64	—	—	
3	7	1[e]			0.29 (−)
1.03	1.52	0.73	—	—	
0.29–3.63	0.57–4.05	0.09–5.94	—	—	
17	28	5[e]		5	0.38 (−)
0.91	0.86	0.51	—	1.73	
0.53–1.54	0.55–1.37	0.20–1.28	—	0.67–4.45	
7	6	2[e]			0.40 (−)
1.03	0.54	0.56	—	—	
0.42–2.50	0.20–1.43	0.12–2.56	—	—	
4[e]	—	3[e]			0.11 (+)
0.67		2.43	—	—	
0.17–2.66		0.50–11.9	—	—	
1[e]	—	—	—	—	0.13 (−)
0.23	—	—	—	—	
0.02–2.21	—	—	—	—	
2	2	2[e]			0.44 (+)
1.44	0.92	3.12	—	—	
0.32–6.40	0.20–4.29	0.63–15.5	—	—	
12	11	4[e]			0.10 (+)
2.44	1.36	1.64	—	—	
1.25–4.75	0.66–2.80	0.55–4.90	—	—	
9	4	1[e]			0.30 (+)
2.96	0.79	0.64	—	—	
1.30–6.74	0.25–2.46	0.08–5.07	—	—	
2	4	2			0.18 (+)
1.28	1.63	2.78	—	—	
0.29–5.69	0.49–5.36	0.56–13.8	—	—	
1	3	1[e]			0.21 (+)
1.96	3.52	3.89	—	—	
0.20–18.8	0.62–19.9	0.34–44.8	—	—	
32[e]		4[e]			0.10 (−)
0.61	—	0.29	—	—	
0.38–0.97	—	0.10–0.83	—	—	

of leukemia (excluding CLL) tended to increase over increasing categories of radiation dose to active bone marrow (Fig. 2), but the trend was not significant ($P = 0.18$). The relative risks (i.e. hazard ratios) for CLL were consistently higher than those for the other leukemias (excluding CLL) which is of interest given that radiation has not been found to increase the risk of CLL (*37*).

Table 5 presents analyses to assess the impact of the choice of analytical strategy on the estimate of risk for all cancers (excluding leukemia), lung cancer and leukemia (excluding CLL). The relative risk (RR) at 100 mSv is presented first for the standard Cox model, which includes all the adjustment factors, and then the RR at 100 mSv is presented for different models depending on the variable to be evaluated. For the standard model, the RR at 100 mSv for all cancers (excluding leukemia), lung cancer and leukemia (excluding CLL) were estimated to be 1.00 (95% CI 0.81–1.24), 0.99 (95% CI 0.86–1.13) and 1.34 (95% CI 0.73–2.45), respectively. The choice of referent population did not have an effect on the estimate of risk; i.e., the RR was

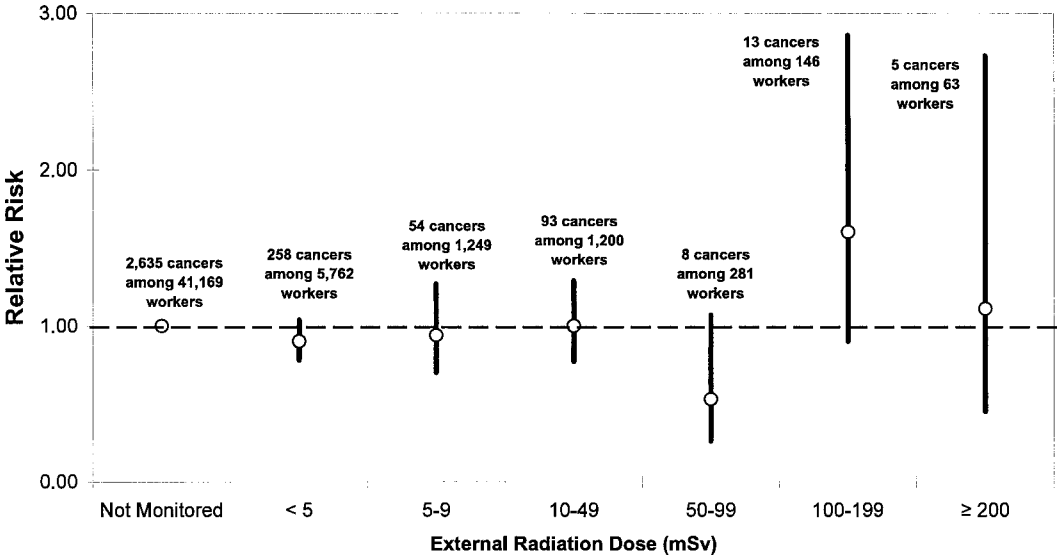

FIG. 1. Intra-cohort relative risk (RR) computations for all cancer combined (excluding leukemia) for workers monitored for radiation over categories of external radiation dose with doses lagged 10 years (Table 4). Number of workers starting each interval presented. Rocketdyne workers not monitored for radiation used as referent. 95% CI presented. *P* for linear trend = 0.45.

similar whether all Rocketdyne workers, all SSFL workers or only monitored workers were analyzed. Restricting the analysis to workers who were not monitored for internal radiation or neutrons or who were not test stand mechanics reduced the estimate of risk but not significantly. Excluding the 292 workers with measurable bioassay or other internal monitoring measurements also failed to influence the measures of radiation risk. Limiting the analyses, however, to include only the dose received at Rocketdyne and excluding the dose received at other facilities resulted in higher estimates of risk; i.e., the RR at 100 mSv for all cancers excluding leukemia increased from 1.00 to 1.11 and for all leukemia excluding CLL from 1.34 to 1.69.

A sensitivity analysis was also conducted to evaluate the possible effect of socio-economic status, duration of employment, gender, age, calendar year and potential exposure to chemicals. No appreciable changes in the RR were seen when adjustment for any of these variables was not made (Table 5).

Relative risk estimates at 100 mSv were also computed for all cancers excluding leukemia, lung cancer and leukemia excluding CLL by attained age, age at exposure,

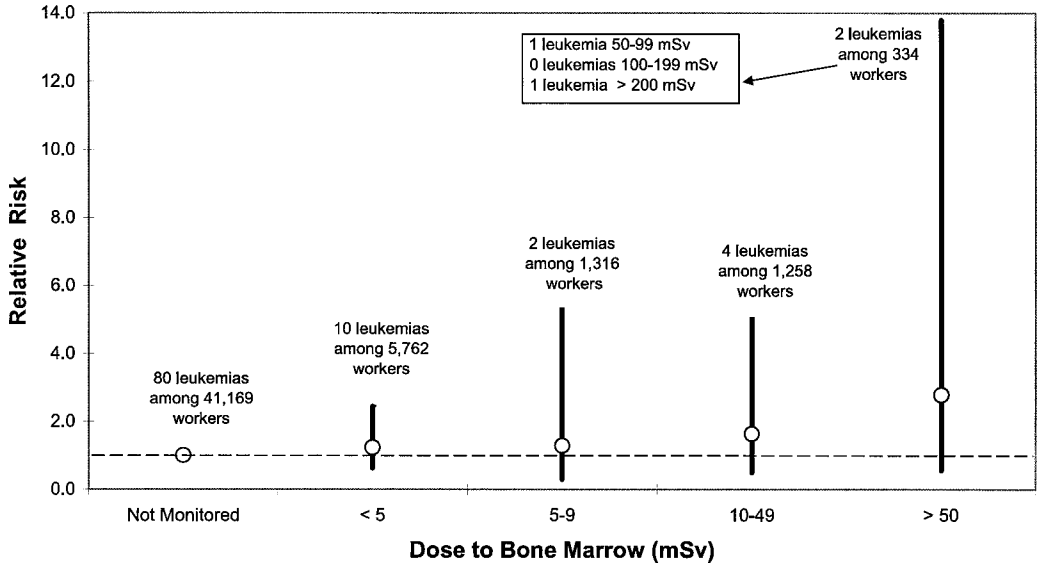

FIG. 2. Inta-cohort relative risk (RR) computations for leukemia (excluding CLL) for workers monitored for radiation over categories of bone marrow dose with doses lagged 2 years (Table 4). Number of workers starting each dose interval presented. Rocketdyne workers not monitored for radiation used as referent. 95% CI presented. *P* for linear trend = 0.18.

TABLE 5
Relative Risk (RR) Estimates at 100 mSv for All Cancers Combined (Excluding Leukemia), Lung Cancer, and All Leukemia Combined (Excluding CLL) Using Alternative Analytical Strategies

Subpopulation	All cancers excluding leukemia			Lung cancer			Leukemia excluding CLL		
	Deaths[a]	RR[b]	95% CI	Deaths[a]	RR[b]	95% CI	Deaths[a]	RR[b]	95% CI
Standard[c]	431	1.00	0.81–1.24	151	0.99	0.86–1.13	18	1.34	0.73–2.45
Study populations									
Monitored workers only[d]	431	1.01	0.82–1.26	151	0.98	0.85–1.13	18	1.34	0.74–2.43
Rocketdyne dose only[d,e]	431	1.11	0.81–1.52	151	0.98	0.84–1.15	18	1.69	0.72–3.96
Restricted dosimetry-internal[d,f]	400	1.00	0.78–1.29	142	1.00	0.64–1.55	16	1.29	0.65–2.58
Unadjusted for test stand work	431	1.00	0.81–1.24	151	0.99	0.86–1.13	18	1.34	0.73–2.46
Unadjusted for pay type	431	0.94	0.75–1.18	151	0.98	0.83–1.16	18	1.33	0.72–2.45
Unadjusted for duration of employment	431	1.02	0.82–1.25	151	0.99	0.86–1.13	18	1.34	0.73–2.45
Unadjusted for gender	431	1.00	0.81–1.24	151	0.99	0.86–1.13	18	1.33	0.73–2.45
Unadjusted for year of birth	431	0.96	0.76–1.21	151	0.99	0.84–1.18	18	1.34	0.70–2.57
Unadjusted for year of hire	431	1.01	0.82–1.25	151	0.99	0.86–1.13	18	1.36	0.76–2.43

[a] Deaths among workers monitored for radiation.
[b] RR at 100 mSv.
[c] Full Cox proportional hazards model with time-dependent measure for exposure and adjustment for year of birth, year of hire, gender, internal monitoring, pay type (hourly/salary), duration of employment, and work as a rocket test stand mechanic. All Rocketdyne workers are included in these analyses, with all non-monitored workers combined as the referent category.
[d] Includes only the 5,801 workers monitored for radiation while working at Rocketdyne.
[e] Excludes any dose received both before and after employment at Rocketdyne.
[f] Excludes the 292 workers with the highest intakes of radionuclides.

time since exposure and different exposure lags (data not shown). No significant differences were observed over categories of attained age, age at exposure or time since last exposure. For leukemia excluding CLL, the RR at 100 mSv was higher at the youngest ages at exposure than at older ages, but the differences were not significant. The RR at 100 mSv also was seen to decrease with increasing lag intervals but not significantly.

DISCUSSION

The absence of any consistent or significant radiation association for any cancer, including leukemia, reflects the relatively low occupational doses experienced by the workers (mean 13.5 mSv) and the relatively small number of radiation workers studied (n = 5,801). Some workers did receive high lung doses (>1 Sv) after intakes of radionuclides, but the number (just over 100) was apparently too small to discern a radiation effect had there been one. A slight increase in leukemia excluding CLL was observed that was consistent with predictions from other radiation studies; however, the increase was not significant, and an even greater increase was seen for CLL, which is not thought to be induced by radiation (*14, 34–37, 45*). Based on small numbers, a positive association between radiation and kidney cancer and a negative association between radiation and bladder cancer were observed, which seem to exemplify the play of chance when so many multiple comparisons are made. Similarly, but based on larger numbers, a positive association for stomach cancer could be contrasted with a negative association for colorectal cancer. The study is noteworthy in that occupational doses received both before and after employment at Rocketdyne were incorporated in the analysis, as were organ doses from the intake of radionuclides (*25, 26*). A large nonexposed worker population was also available for comparison.

The occupational doses received by most workers in this study (mean 13.5 mSv) were much lower than what they received from natural background sources of radiation during their lifetimes (of the order of 180 mSv) and from medical sources of radiation (of the order of 30 mSv) (*14*). Detecting a radiation effect from a low occupational dose in the presence of much larger natural and man-made sources is problematic, and the play of chance, bias and confounding takes on a more important role than when exposures are high.

Comparisons with Previous Radiation Studies

Studies of workers in the nuclear industry have not found consistent associations between radiation and increased cancer risks, but the power of the studies has been limited by the relatively low doses received and/or the small study sizes. Large combined studies of workers in the United States have not reported increases in leukemia, the malignancy that can occur as early as 2 years after exposure and that is most frequently seen in populations exposed to high doses (*1, 14*). In a large combined study of workers in three countries, a significant excess of leukemia was reported but only at one facility and at a cumulative dose greater than 400 mSv (*12, 38*). No increase in solid cancers was observed (*12*). In an expanded 15-country study (*13*), the risk

of leukemia was no longer significant, and for the first time a significant risk for solid cancers was reported. However, confounding by tobacco use was likely since the solid cancer increase was due entirely to an abnormally high risk of lung cancer (*39*). Further, the cancer excess appeared concentrated in only one of the 15 counties.

Large studies of workers in the United Kingdom, Canada and Japan and of workers at U.S. navy shipyards and in the U.S. nuclear industry also have failed to find significant increases in leukemia (*3–6, 8, 10, 40, 41*). A recent follow-up of workers at the Portsmouth Naval Shipyard reported a significant dose–response trend for leukemia (*42*). However, the report is difficult to interpret because CLL was apparently included in the analysis, the exposed workers did not have an elevated risk of leukemia but rather the referent group had a significantly low risk, and a previous case-control study within the cohort had linked leukemia elevations to solvent use and not radiation (*43*). The most recent analysis of the Portsmouth Naval Shipyard study adjusted for potential confounders such as organic solvents, and the excess of leukemia, which still included CLL, was no longer significant (*44*). Issues of potential study biases and confounding become increasingly important when the radiation dose and corresponding risk are low (*9*).

Increased risks of leukemia have been reported among workers at the Mayak facility in Russia but only at cumulative external doses in excess of 1 Sv and not among workers exposed primarily to plutonium (*15, 16, 20*). In our investigation, the average cumulative bone marrow dose, including external and internal contributions to dose, was only 14 mSv, and no bone marrow dose exceeded 1 Sv. For all monitored workers in our study, the SMR for CLL was 2.25 ($n = 7$), whereas for leukemia excluding CLL it was lower (SMR 1.21; $n = 16$). For leukemia excluding CLL, the relative risk at 100 mSv was estimated as 1.34 (95% CI 0.73–2.45) and was in line with what might be predicted from other studies of higher exposures (*14, 37, 45*). Nonetheless, the increase was not significant, and the higher risk seen for CLL, which is not considered radiation inducible, adds caution to a causal interpretation.

Except for underground miners exposed to high levels of radon (*46*) and Mayak workers who inhaled high levels of plutonium (*16, 47–49*), increased lung cancer risks have not been consistently or convincingly identified among occupationally exposed workers (*14, 36*). No increases were observed in the international study of workers in three countries or in studies of U.S., Japanese or UK workers (*1, 5, 6, 10, 12, 50*). Combined studies of 120,000 non-mining workers involved with uranium processing and fabrication have also failed to reveal any increases in lung cancer or any other cancer (*51*). A comprehensive case-control study of 787 lung cancer cases among workers at three uranium processing plants in the United States also revealed no significant association with lung doses up to 250 mGy (*52*). The one exception to the absence of a lung cancer excess is the recent 15-country study where smoking may have played a role (*13, 39*). In our investigation, the average cumulative lung dose was 19 mSv (range 0–3,000 mSv) and apparently too low to expect to detect a radiation effect had there been one; the relative risk at 100 mSv was estimated as 1.0, and RRs higher than 1.13 could be excluded with 95% confidence.

Studies of radiation workers in the United Kingdom had reported an association between the intake of radionuclides and prostate cancer (*53*), but no similar association was seen among Rocketdyne workers who were monitored for internal radiation exposures. A recent mortality study of workers in the U.S. nuclear industry (*41*) reported remarkably low SMRs for all causes of death (SMR 0.41), which is not comparable with our Rocketdyne study (SMR 0.80) or, it seems, with any other study of radiation workers; e.g., the all-cause SMRs for the large Hanford and UK worker studies were both 0.82 (*6, 50*). The mean dose (25.7 mSv) for the U.S. nuclear power industry study (*41*) was low and similar to that of the Rocketdyne study (14 mSv), and no significant increases in leukemia or solid cancers were observed in either study. However, a highly significant association and high radiation risk was reported for deaths from heart disease in the U.S. nuclear utility study (*41*) which also was incompatible with the absence of an association in our study and in other larger studies in the United Kingdom and United States (*6, 50*). An association between radiation and heart disease of borderline significance was reported in the three-country study of workers, but the authors attributed the finding to residual confounding by lifestyle factors for which their SES variable was an inadequate proxy or to chance when making multiple comparisons (*12*). Low-dose radiation exposures are unlikely to be related to heart disease (*54*).

Comparisons with Previous Rocketdyne Study

Our study is an independent look at the mortality experience of the Rocketdyne workforce and essentially started from scratch in identifying the study base, conducting dosimetry evaluations, and performing tracing activities. In addition, we expanded the previous investigation by 5 years (*22–24*). In contrast to the previous study, we did not find significant associations with radiation dose for all cancers, lung cancer, hemato- and lymphopoietic cancers (ICD 200–208) or aerodigestive cancers (ICD 140–151). The previous investigators recognized the small size of the population studied and the low occupational doses received and concluded that their findings would have to be confirmed by other studies and/or further follow-up of the Rocketdyne workforce (*24, 55*). The differences in findings between the two studies may be related to the additional years of follow-up coupled with differences in study design and the approach to dose assessment and analysis. Different criteria for worker selection and eligibility resulted in our study population being larger than the previous one by 1,194 (or 25.9%) workers. The number of workers monitored for in-

ternal radiation (2,232 compared to 2,297) was similar, but the number of workers monitored for external radiation (5,743 compared to 4,563) was appreciably larger in our study. The increased numbers of workers and longer follow-up (161,605 person-years compared to about 119,100) resulted in an additional 593 deaths from all causes (a 67.8% increase) and an additional 198 deaths from all cancers (a 76.7% increase). Another important difference was that the previous investigation limited their analysis to radiation doses received only at Rocketdyne, whereas we included additional occupational doses received elsewhere by over 32% of the radiation workers. The collective dose increased by 35% when doses received elsewhere were included (*25*). Excluding such exposure could produce imprecise or spurious results; in fact, higher radiation risk coefficients did result when doses received elsewhere were excluded from our analysis. Further, we computed internal radiation doses for each organ after the intake of radionuclides, whereas the previous investigation assumed lung dose to be a surrogate for internal doses received by all organs.

The previous study reported a significant threefold increased risk of all cancers among workers exposed to greater than 200 mSv external radiation based on four cancer deaths (*24*), whereas we failed to find a significant elevation based on five cancer deaths (RR 1.11; 95% 0.5–2.7) or a significant dose–response trend ($P = 0.45$). Similarly, we failed to confirm the previously reported significant fourfold increase of lung cancer at >200 mSv (based on two deaths) (*24*); our estimate of RR was 1.73 (95% CI 0.7–4.5) based on five deaths, and no dose–response trend was apparent ($P = 0.38$). A significant trend also had been reported previously for all lymphatic and hematopoietic malignancies taken together (excluding CLL) based on 28 deaths (*24*) that was not seen with further follow-up and 51 deaths ($P = 0.12$). Such an aggregated category, however, is not very informative because it includes Hodgkin lymphoma, non-Hodgkin lymphoma and multiple myeloma, which have not been convincingly or consistently found to be increased after radiation exposure (*14, 34, 45, 49, 56*). Further, because hematological and lymphoprolific malignancies have different etiologies, combining them as a single entity other than for descriptive purposes is not commonly done in studies of radiation-exposed populations (*6, 12, 34*), and the rationale for doing so has been questioned (*57*). The previous findings were based only on radiation doses received while employed at Rocketdyne, which apparently resulted in higher estimates of radiation risk than when analyses included total career dose.

The earlier investigation reported high relative risks at cumulative lung doses greater than 30 mSv from inhaled radionuclides for lymphopoietic cancers excluding CLL and for upper aerodigestive tract cancers (ICD 140–151; i.e., cancers of the mouth, esophagus and stomach) but not for lung cancer (*24*). These analyses are difficult to interpret because cumulative lung dose from inhaled radionuclides was used as a surrogate of dose to other organs. Depending on the radionuclide inhaled, some tissues such as esophagus or bone marrow would receive miniscule doses whereas the lung burden could be high (*25*). Further, since practically all workers monitored for radionuclides also received external exposure and many also had received exposures at places of employment other than at Rocketdyne, the estimate of cumulative lung dose only from internal exposure must be an incomplete surrogate for doses to other organs. The number of aerodigestive cancers (ICD 140–151) increased from 14 (*23*) to 41 in our study, and no significant elevations or trends ($P = 0.49$) were observed. Restricting our analysis to only those workers monitored for internal radiation but including all external radiation doses received at Rocketdyne or elsewhere also did not reveal any significant dose-response trends for lung cancer (the organ that received the highest doses overall) or any other cancer.

Strengths and Limitations

The strengths of our investigation include the nearly complete follow-up of the workforce, the approach to obtain dose information from all places of employment, the inclusion of doses to specific organs after the intake of radionuclides, and the availability of a large nonexposed worker population for comparison. Vital status (either death or confirmed alive) was determined for nearly 98% of the workers. The follow-up was up to 50 years (27.9 years on average), providing ample time for any radiation excess to manifest itself given that there was one. Over 32% of the workers had received radiation exposure at facilities other than at Rocketdyne, and we were able to incorporate these occupational doses to create a lifetime career dose. We also were able to incorporate organ-specific doses after the intake of 14 different radionuclides by applying ICRP models to the available bioassay monitoring data (*25*). Further, the potential for exposure to chemicals associated with the testing of rocket engines could be controlled for in the analyses because of the existence of detailed job history work records. The major limitations, however, are the low doses and small study size. Other limitations, such as incomplete smoking histories, are described below.

1. Smoking

The absence of detailed smoking information is also a limitation, but indirect methods were used to evaluate possible confounding. It was seen that pay type was a predictor of cancer risk, with somewhat higher risk of cancers of the lung and of smoking-related sites seen for hourly compared to salaried workers. This difference is often seen in occupational studies (*58*) and likely reflects different patterns in the use of tobacco products by blue collar (hourly) compared to white collar (salaried) workers (*59*). Over the past 20 years, the prevalence of cigarette smoking has declined in the general population and among white collar workers but not among blue collar workers, who continue to smoke

in large numbers (*60, 61*) and at a rate twice that of white collar workers (*62*). We controlled for pay type in the internal dose–response analyses to account for possible differences in smoking and other characteristics between hourly and salaried workers.

To obtain additional information on smoking histories and the possible association with pay type, a brief smoking survey was conducted of a random sample of nearly 300 living workers equally divided by pay type (hourly/salaried). Compared to salaried workers, hourly workers were significantly more likely to have smoked cigarettes (61% compared to 41%), to have started smoking at a younger age, to have quit working at an older age, to smoke for more years, and to have consumed more cigarettes during their lifetime in terms of ''pack-years''. The survey was limited, because only survivors were included and the response rate was low, only 50%. Nonetheless, it supports the importance of controlling for pay type in the analyses as a surrogate measure of smoking.

2. Pay type and race

Other limitations include an imperfect categorization of pay type; e.g., we classified anyone who held an hourly job for at least 20% of his or her career as an hourly worker. Race also could not be determined for 13% of the workers. Race was explored as an adjustment factor in the Cox analyses but ultimately was not included in the models because it did not affect the exposure estimates in any appreciable way. Conducting analyses only on white males also did not materially change the estimates of radiation risk.

3. Dosimetry sources

The completeness of the various dosimetry sources was not evaluated. Landauer, Inc. is the largest provider of dosimetry services in the world, but there are others that were not accessed. The Nuclear Regulatory Commission resource was likely complete because of legal requirements and presumably the Department of Energy databases, but neither were designed for epidemiological research, nor were the U.S. military databases. The U.S. Navy database was the only major source that we were unable to access, but we did obtain notifications of prior radiation exposure in the Navy from the Rocketdyne worker records. We sought radiation exposure information for all Rocketdyne workers and not just for the 5,801 workers monitored for radiation at Rocketedyne. Only 3.6% of the non-monitored workers were monitored elsewhere, and their average dose was low (2.6 mSv). Analyses including or excluding these workers produced similar results. Although we were successful in accessing the major dosimetry databases in the United States, some exposures for a small number of workers were likely missed. However, the amount of missed dosimetry information is likely to be small since so many databases were accessed and so many of the databases were overlapping.

4. Comparisons with general population

Mortality comparisons with the general population are commonly made in occupational studies to identify patterns of risk that might be tied to specific exposures. However, there are potential biases in these comparisons because of differences related to health status, selection processes and lifestyle factors that cannot be controlled for in the analysis. There were other uncertainties in the SMR analyses associated with differences in race and place of birth. It is unlikely that the racial mix of the state of California (in terms of the broad classifications of white and non-white populations used in the analysis) is comparable to that of the working Rocketdyne populations over the 50-year study period. In addition, nearly 25% of the over 11,000 deaths occurred outside the state of California, indicating the mobility of the workforce after retirement as well as differences in the study base; i.e., the California population was used for comparison, yet a substantial proportion of the worker population lived in other states. We conducted SMR analyses based on other general population groups, and the patterns were the same, although the magnitude of the SMRs differed. When comparisons were made with the U.S. general population, the SMRs were substantially lower than those computed from the state of California, with the SMRs for all cancer, lung cancer, leukemia and almost all causes being significantly low. When comparisons were made with rates available for Los Angeles and Ventura Counties (where many of the workers had lived when employed), the SMRs were similar to those computed using rates for the state of California.

Although the choice of the general population comparison group is somewhat arbitrary, it is the internal (intracohort) analyses that are most appropriate when evaluating whether a radiation association is present in this population. In this study, Rocketdyne workers were also compared with each other. For some analyses, the referent group was taken as those workers with <5 mSv cumulative dose; in other analyses, the referent was all workers who were not monitored for radiation but worked for the same company under presumably similar conditions and medical care opportunities. Thus any noncomparability present when comparisons are made with the general population was reduced.

5. Different analytic strategies

Despite the absence of any significant associations, it was informative to evaluate various analytic strategies to learn whether they had appreciable effect on the estimate of risk. Age, calendar year, gender, pay type, internal monitoring, and work as a rocket test stand mechanic were evaluated in addition to duration of employment. No appreciable differences were seen, indicating that these factors were unlikely confounders in the dose–response analyses. For completion, an analysis was undertaken to learn whether radiation risks might differ by age at exposure, age of observation, or dose lag. Few differences were seen, and none

were statistically significant. The absence of a difference with dose lags likely reflects the fact that most exposures occurred many years ago, and there were thus relatively few workers with substantial doses received even 20 years prior to the end of study.

6. Healthy worker effect

The healthy worker effect was not as apparent in this population as seen in others, perhaps because the majority of workers were employed prior to 1970 and the selection effects for employment are often seen to diminish over time and especially for cancer (*59*). Significantly low risks remained, however, for all causes of death, all cancers combined, heart disease and external causes of death when compared with the general population of California.

Conclusion

No consistent associations between cancer and radiation were found within the Rocketdyne workforce followed for up to 50 years. Comparisons with the general population of California revealed a healthy workforce with overall death rates significantly low (SMR 0.79). Cancers of *a priori* interest, i.e. lung, leukemia and kidney, were not significantly associated with radiation. The methods used, however, indicate the importance of capturing complete occupational histories from existing dosimetry databases and in computing organ-specific doses from available bioassay monitoring records on radionuclide intake. The study is limited by the small sample size and relatively low cumulative occupational doses.

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