Differences in Mortality by Radiation Monitoring Status in an Expanded Cohort of Portsmouth Naval Shipyard Workers

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Studies of leukemia and lung cancer mortality at the Portsmouth Naval Shipyard (PNS) have yielded conflicting results. In an expanded cohort of PNS workers employed between 1952 and 1992 and followed through 1996, the all-cause standardized mortality ratio (SMR) was 0.95 (95% confidence interval, 0.93–0.96). Employment duration SMRs were elevated with confidence intervals excluding 1.00 for lung cancer, esophageal cancer, and all cancers combined. Leukemia mortality was as expected overall, but standardized rate ratio analyses showed a significant positive linear trend with increasing external radiation dose. The role of solvent exposures could not be evaluated. Findings differed by radiation monitoring subcohort, with excess asbestosis deaths limited to radiation workers and several smoking-related causes of death higher among nonmonitored workers. At PNS, asbestos exposure and possibly smoking could be nonrandomly distributed with respect to radiation exposure, suggesting potential for confounding in internal analyses of an occupational cohort. (J Occup Environ Med. *2004;46:677–690*)

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Workers at the Portsmouth Naval Shipyard (PNS) in Kittery, Maine, have been subjects of a number of epidemiologic investigations, beginning with a report by Najarian and Colton[1] of elevations in proportionate mortality from leukemia and from all cancers combined. A subsequent cohort mortality study at this facility conducted by the National Institute for Occupational Safety and Health (NIOSH) studied 24,545 white male workers ever employed at PNS between January 1, 1952, and August 15, 1977, and found no excesses of leukemia or overall cancer mortality.[2] The initial findings of Najarian and Colton were attributed to misclassification of radiation exposure for deceased workers. However, an elevated lung cancer standardized mortality ratio (SMR) was observed among workers with at least 1 rem cumulative external radiation exposure and at least 15 years' latency,[3] and elevated leukemia mortality was seen in workers exposed to at least 1 rem (10 mSv), with no latency requirement.[4] NIOSH pursued the lung cancer finding in a case-control study and found that adjustment for 2 potential confounding exposures, asbestos and welding fume, yielded somewhat diminished risk estimates for radiation exposure.[3] A leukemia case-control study[4] found no statistically significant associations between radiation or solvent exposure and leukemia, but showed elevated odds ratios for leukemia mortality among electricians and welders.

The current study expands the PNS cohort to male and female workers of all races employed at the shipyard between January 1, 1952, and December 31, 1992, with vital status follow up through 1996. This update extends follow up to at least 19 years for each member of the original cohort still alive at the end of follow up. These modifications facilitate additional evaluation of differences between radiation-monitored subcohorts and their nonmonitored counterparts observed in earlier studies.[5] The full cohort now totals 37,853 workers, with a subcohort of 13,468 workers monitored for radiation at PNS. Of the radiation-monitored workers, 11,791 received a recorded dose greater than zero (representing a measured dose greater than the limit of detection) at the shipyard.

Description of Exposures

The PNS was established in 1800 to design, build, and overhaul many kinds of ships.[6] After 1917, the shipyard increasingly concentrated on building and overhauling submarines. The shipyard began to perform nuclear work in the 1950s and launched its first nuclear submarine in 1957. The shipyard continued to build, overhaul, and repair nuclear submarines until 1971, when new construction ceased, leaving only overhaul and repair functions, which continue today.

Radiologic Exposures

Details of radiologic exposures at PNS and the procedures for assembling and validating dosimetry data for this study are described elsewhere.[6a] At PNS, the primary exposure results from external whole-body penetrating gamma radiation emitted by long-lived radionuclides deposited in reactor systems and components. Relatively high-energy gamma rays (>100 keV) constitute the major exposure.

In 1950, PNS instituted a limited personnel dosimetry program for recording worker doses to penetrating gamma radiation. An expanded, structured external monitoring program began in 1958. To become "qualified" radiation workers, employees had to pass a medical examination and complete a radiation safety training program. Workers who fulfilled these requirements were issued a personnel radiation dosimeter when they required access to radiation-controlled areas of the shipyard, both on board submarines and in support buildings.

Before 1959, shipyard exposures were limited to occupations involving industrial radiography, instrument maintenance and calibration, and medical programs, with the exception of limited reactor power testing conducted in 1958. Both radiation monitoring and the collective dose increased with the introduction of overhaul and refueling activities in 1959. The upward trend in collective dose continued through 1965 with a few exceptions. The collective annual dose surpassed 29 Sv in 1965, and the number of monitored workers peaked at just over 3800 in 1967.[6a] Since 1965, there has been a decline in the annual collective dose as a result of improvements in submarine design and worker safety programs, although the number of radiation workers initially remained high. The cumulative dose distribution is best approximated by the hybrid-lognormal distribution described by Kumazawa et al.[7] The distribution deviates from lognormal in the high-dose range as a result of administrative dose limits imposed by the shipyard and in the low-dose region as a result of the practice of recording "zero" dose values for actual doses less than the minimum measurement sensitivity.[6a]

A number of workers (822) received doses outside of PNS employment, including 7 workers who were not monitored at the shipyard. When a dose of record was not available for individuals who had likely incurred prior radiation exposure, PNS staff administratively assigned the maximum legal dose for each quarter a worker was known to have worked in a radiation environment, even though the actual exposure was likely to have been much less. NIOSH staff investigated and made adjustments to better reflect the exposure potentials of events triggering administratively assigned doses.[6a] With these adjustments, the collective dose was 277.42 person-Sv through 1996, with 96.8% attributable to exposures at the shipyard and the remainder to off-site exposures. The mean and median doses from shipyard exposures alone were 19.95 mSv and 2.90 mSv, respectively, compared with 20.59 mSv and 3.24 mSv, respectively, when recorded off-site dose is included.

Nonradiologic Exposures

PNS is a large industrial complex. Throughout the modern history of the shipyard, processes have included insulating and pipefitting, mechanical repair and maintenance, electrical and instrument work, rigging, welding and cutting, painting, chipping, caulking, abrasive blasting, metal work, woodwork, plastics and rubber work, and foundry work. Certain occupational groups were potentially exposed to known or suspected lung carcinogens such as asbestos, silica, and welding fume. Known or suspected leukemogens used at the site include organic solvents such as benzene and carbon tetrachloride. Although the use of these 2 solvents at the shipyard was strongly restricted by the mid-1950s, the potential for low-level exposure to benzene-containing petroleum distillates such as gasoline continued. Because much of the radiation work at PNS took place onboard submarines, where enclosed spaces are common, it is possible that potential for exposure to asbestos and certain other contaminants was higher in these areas than in nonradiation areas. However, this possibility cannot be evaluated in the context of this full cohort study.

The PNS medical clinic monitored various chemical hazards starting in

the 1940s, with more intensive monitoring beginning in the late 1970s. Unfortunately, detailed work histories as well as data on these chemical exposures are not available in electronic format, a limitation that prevents assessment of nonradiologic exposures in the full cohort.

Study Design and Methodology

Cohort Definition

The study population comprises males and females of all races employed as civilian workers at PNS for at least 1 day between January 1, 1952, and December 31, 1992. The shipyard began to maintain a complete set of records identifying the PNS workforce in 1952. Assembly of the cohort of workers employed through August 15, 1977, has been described previously.[5] For the current update, PNS staff provided hardcopy and electronic lists for identification of workers hired after the cutoff date (August 15, 1977) of the initial study. Females and nonwhite males employed before August 1977 were also identified from these sources and included in the expanded cohort.

We also required that the following dates be available for each worker: date of birth, hire date, termination date, and date of death, if the worker was known to be deceased. Two hundred ninety-six workers (0.8%) were eliminated from the master roster because these dates could not be obtained. Two workers, one of whom had previously worked as a radium dial painter, were excluded because their radiation exposures could not be evaluated. The final cohort includes 37,853 workers, 13,468 of whom have records of being monitored for external radiation exposure at PNS.

Vital Status Ascertainment

Vital status was updated through December 31, 1996. For the cohort of workers employed through August 1977, death certificates were obtained from the states.[5] Members of the expanded cohort not known to be deceased were submitted to the National Death Index (NDI) service of the National Center for Health Statistics. NDI Plus[8] returns coded cause of death for deaths occurring in 1979 or later. The full cohort was also submitted to the Social Security Administration (SSA) for a "presumed living" search, which provides date of death information both before and after 1979 and also confirms alive status for those paying social security taxes or receiving social security benefits. Death certificates were sought from the state in which the death occurred for all persons determined to be dead from the SSA results who were not found on the NDI search. Death certificates from both time periods were sent to a qualified nosologist for coding to the International Classification of Disease–Adapted (ICDA) revision in effect at time of death.

For 207 workers (1.7% of all deaths), we had a date of death but were unable to ascertain the cause of death. These deaths were retained in the all-cause SMR analyses and were included in the "other unspecified" cause of death category. Only underlying cause of death was considered in the analyses. When vital status remained uncertain (n = 1339, 3.5%), subjects were considered to be alive, an assumption that could lead to an underestimate of the SMR.

Radiation Exposure Assessment

Reported external radiation dose records for each monitored worker were obtained from the site. As described by Daniels et al,[6a] adjustments were made for administrative dose. Because only annual radiation doses were readily available, each worker was assumed to have received that dose at a constant rate throughout the year. Therefore, each individual's yearly dose was divided into equal dose-days. Because internal and neutron exposures constitute a minor portion of the collective radiation dose, internal exposures were not incorporated in this study and neutron dose was not separated from the gamma dose.

Standardized Mortality Ratio Analyses

The NIOSH personal computer Life Table Analysis System (PC-LTAS, version 1.0d) was used to generate expected numbers for all deaths, all cancer deaths, and cause-specific deaths for each race and sex within 5-year age and 5-year calendar time periods.[9] Expected and observed deaths were accumulated for each of these age and calendar time periods from January 1, 1952, through December 31, 1996.

Expected numbers of deaths were based on U.S. population death rates specific for the race, gender, and 5-year age and calendar time periods, applied to the number of person-years at risk of dying. U.S. expected rates were based on deaths from 1940 forward except for asbestosis and silicosis, causes for which rates were only available from 1960 forward. For these outcomes, enumeration of observed deaths and person-years at risk began in 1960 as well. Numbers of deaths observed for each cause were divided by the expected number of deaths to obtain cause-specific standardized mortality ratios. The precision of each estimated SMR was assessed assuming a Poisson distribution, with 2-sided 95% confidence intervals.

Because differences between mortality of the shipyard population and that of the U.S. population could be in part the result of regional (nonoccupational) differences, we also compared mortality in the full cohort with combined death rates from Maine and New Hampshire. Combined, these 2 states account for 70% of deaths to date in the cohort. For these states, rates for all outcomes are available only from 1960 forward, so both observed and expected deaths were calculated from that point. In the LTAS analyses, comparison population rates are presumed to be invariant, leading to a

slight underestimate in uncertainty, which would be greater in the combined Maine–New Hampshire comparison.

Subcohorts

The PNS cohort was previously divided into 3 subcohorts delineated by radiation monitoring status and cumulative dose received at PNS as a civilian employee.[5] Workers' allocation among these cohorts was allowed to change over time, with workers moving from nonmonitored to radiation worker status and from unexposed radiation worker status to exposed radiation worker status as monitoring status or accumulated dose changed. However, summary statistics presented here allocate workers to the last subcohort to which each was assigned.

With the addition of nonwhite and female workers and the extension of date of first employment cutoff to December 31, 1992, the "exposed radiation workers" group (previously subcohort I) now comprises 11,791 radiation-qualified workers with cumulative dose above zero. The largest group, nonmonitored workers (previously subcohort II), includes 24,385 workers never monitored for radiation while they were civilian employees of PNS. An additional 1677 workers (subcohort III) were radiation-qualified and received dosimeters but never had a recorded dose above zero. Normally, if a worker was monitored, a zero was entered in the annual summary if no dose was detected above the limit of detection. Although these workers could have received a dose below the limit of detection of the monitoring equipment, they are referred to as "unexposed" radiation workers for consistency with earlier reports. Subcohorts I and III are referred to collectively as "monitored" or "radiation" workers. Workers monitored only between 1962 and 1964 who never received a nonzero dose would not have a radiation record. These workers are allocated to subcohort II (nonmonitored workers) instead of subcohort III. Seven people who had reported an off-site dose (ranging from 0.03–9.97 mSv cumulative exposure) but were not monitored as PNS civilian employees are included in the nonmonitored group.

For all workers, person-years at risk were started at January 1, 1952 (study begin date) or the date of first employment at the shipyard, whichever was later. Person-years-at-risk were ended on the date of death or December 31, 1996, whichever came first.

To assess whether PNS mortality outcomes were affected by duration of employment, we conducted separate analyses for workers within each subcohort employed for at least 5 years, the median length of employment for nonmonitored workers. Detailed work histories were not available for the full cohort and gaps in work history could not be assessed. Duration of employment was determined by the difference between the initial employment date and the final termination date or end of study, whichever was earlier. For workers employed at the shipyard before 1952, person-years at risk began in 1952, but actual employment dates were used for all duration and time since exposure analyses.

Finally, we reexamined the original cohort of white males employed at the shipyard as of August 15, 1977, to see how the additional follow-up time had affected the cohort's mortality experience and to see how that cohort compares with the expanded cohort.

Internal Analyses

Because SMRs are affected by the age structure of the study population, comparison of SMRs for different populations can be misleading. Standardized rate ratios (SRRs) allow for comparison among populations by weighting observed stratum-specific rates according to a common (internal) standard.[10] To confirm that differences observed between subcohorts in the SMR analyses were not merely artifacts of differences in age distributions, we examined SRRs by subcohort with nonmonitored workers as the baseline for comparison.

A second set of SRR analyses was performed to assess the associations between exposure levels and mortality outcomes. For these analyses, person-years were further stratified by cumulative external radiation exposure. Cumulative exposure strata of 0–<1, 1–<10, 10–<50, and >50 mSv were chosen to facilitate comparability with previous analyses.[3,5] To examine trends by levels of exposure, we used the lowest dose group, which included both unexposed radiation workers and those with a cumulative dose less than 1 mSv, as the baseline and compared their mortality experience with that of workers in each of the other cumulative dose categories. Dose-response analyses were conducted with and without adding dose received outside of PNS civilian employee status. LTAS also generates Taylor series-based confidence intervals for each specific SRR. For dose-response analyses, a linear trend is calculated in a person-year-weighted regression of directly standardized rates.[11] Statistical significance of each trend was determined using a 2-tailed z-test with an alpha of 0.05.

Outcomes of Interest

Cancers of a priori interest included lung cancer and leukemia. Because lung cancer has been strongly associated with smoking, the potential for smoking to confound relations observed between radiation exposure and this outcome must be addressed. Smoking data are available only for a subset of this cohort, and the size of the cohort prevented ascertainment of smoking status at the individual level. Instead, to gauge whether smoking was likely to be differentially distributed with respect to radiation monitoring status (and dose), we examined the SMRs for other causes of death likely to be elevated in a smoking population: nonmalignant respiratory diseases other than asthma and pneumonia,

and smoking-related cancers other than lung cancer. Smoking-related cancers have previously been defined as including malignancies of the oral cavity and pharynx, larynx, esophagus, bladder, renal pelvis, and pancreas.[12] As a result of limitations of the LTAS system, we included all kidney cancer.

Because of the potential for confounding of lung cancer findings by exposures to asbestos and silica (known exposures at the site), we examined death from asbestosis and silicosis as well. Solvent exposures also occurred at the site. Therefore, we evaluated deaths from anemias of other/unspecified type (nonpernicious). Liver cancer was not of particular a priori interest, but after finding elevations in malignant neoplasms of the liver unspecified as to primary or secondary status, we examined mortality for liver cancer, cirrhosis, and alcoholism to determine whether the excess in the unspecified category was mirrored by increases in these related causes or was more likely the result of underascertainment. Lags of 0, 2, and 5 years were used for leukemia analyses and lags of 0, 10, 15, and 20 years for lung cancer and other cancers of longer latency. Lags of 10, 20, and 30 years were used for asbestosis analyses.

Results

Descriptive Statistics

Full Cohort. The full cohort comprises 37,853 workers, including 32,771 males and 5082 females (Table 1). Only 87 workers (0.3%) of known race were nonwhite, with 27,703 white and 10,065 of unknown race. For the analyses, workers of unknown race were assumed to be white. At the end of vital status follow up, approximately two thirds (25,460) of the workers were classified as alive (including 1339 workers of unknown vital status) and one third (12,393) as deceased.

Subcohorts. Nonmonitored workers comprise 64% of the total PNS workforce. The 11,791 exposed radiation workers account for an additional 31% of the cohort. Exposed radiation workers were more likely than nonmonitored workers to be male (98% vs. 80%) and alive (73% vs. 65%) at the end of follow up. However, monitored workers were born later, on average, than nonmonitored workers (Table 2). Of unexposed radiation-monitored workers, who had the earliest average birth year, 62% were alive and 98% were male.

The average employment durations for monitored and nonmonitored workers were quite different. Monitored employees worked almost twice as long as their nonmonitored counterparts, on average. Differences in median employment duration were even greater. Although more than three fourths of radiation workers were employed at PNS for at least 5 years, this figure drops to half for nonmonitored workers. Nonmonitored workers outnumbered exposed radiation workers by more than 2 to 1. Age at first employment was similar for all 3 subcohorts.

Within the radiation-monitored subcohorts, the number of years monitored, as well as the portion of

TABLE 1
Portsmouth Naval Shipyard Cohort and Subcohort Demographics and Vital Status as of December 31, 1996

	Alive	Deceased	Unknown*	Total
Full cohort				
Male	20069 (61.2%)	11910 (36.3%)	792 (2.4%)	32771 (86.6%)
Female	4052 (79.7%)	483 (9.5%)	547 (10.8%)	5082 (13.4%)
Total	24121 (63.7%)	12393 (32.7%)	1339 (3.5%)	37853 (100%)
Exposed radiation workers				
Male	8140 (70.7%)	3217 (28.0%)	150 (1.3%)	11507 (97.6%)
Female	277 (97.5%)	6 (2.1%)	1 (0.4%)	284 (2.4%)
Total	8417 (71.4%)	3223 (27.3%)	151 (1.3%)	11791 (100%)
Unexposed radiation workers				
Male	990 (60.1%)	637 (38.7%)	19 (1.2%)	1646 (98.2%)
Female	30 (96.8%)	1 (3.2%)	0 (0%)	31 (1.8%)
Total	1020 (60.8%)	638 (38.0%)	19 (1.1%)	1677 (100%)
Nonmonitored workers				
Male	10939 (55.8%)	8056 (41.1%)	623 (3.2%)	19618 (80.5%)
Female	3745 (78.6%)	476 (10.0%)	546 (11.5%)	4767 (19.5%)
Total	14684 (60.2%)	8532 (35.0%)	1169 (4.8%)	24385 (100%)

* Grouped with workers known to be alive in analyses.

tenure at PNS during which the worker was monitored, varied by cumulative dose category (Table 3). Average tenure at PNS was similar across dose categories, except for workers in the highest dose category, who worked somewhat longer. However, the number of years monitored and percent of employment in radiation worker status increased with cumulative dose category.

Standardized Mortality Ratio and Standardized Rate Ratio Results: Full Cohort and Monitoring Subcohorts

A U.S. Population Comparison. All-cause mortality in the full cohort was slightly lower than would be expected from U.S. population rates (SMR = 0.95; 95% confidence interval [CI] = 0.93–0.96; number of deaths (*n*) = 12,393). The nonmonitored cohort had an all-cause SMR of 0.97 (95% CI = 0.95–0.99, *n* = 8532). In contrast, both monitored subcohorts exhibited lower SMRs, 0.90 for the exposed subcohort (95% CI = 0.86–0.94, *n* = 3223) and 0.87 for the unexposed radiation worker subcohort (95% CI = 0.80–0.95, *n* = 638).

In the full cohort, fewer deaths than expected occurred for several nonmalignant causes of death, including respiratory tuberculosis (SMR = 0.29; 95% CI = 0.15–0.52, *n* = 11), diseases of the heart (SMR = 0.94; 95% CI = 0.91–0.96, *n* = 4815), circulatory system (SMR = 0.90; 95% CI = 0.85–0.95, *n* = 1121), and digestive system (SMR = 0.88; 95% CI = 0.80–0.96, *n* = 484), as well as for accidents (SMR = 0.70; 95% CI = 0.64–0.77, *n* = 433) and violence (SMR = 0.77; 95% CI = 0.68–0.88, *n* = 246).

In contrast, cancer deaths were slightly elevated in the full cohort (SMR = 1.06; 95% CI = 1.02–1.10, *n* = 3192), primarily as a result of an excess in the nonmonitored subcohort (SMR = 1.06; 95% CI = 1.01–1.10, *n* = 2069) and among exposed radiation workers (SMR = 1.07; 95% CI = 1.00–1.14, *n* = 950). Cancer deaths were closer to the expected among unexposed radiation workers, who had an SMR of 1.01 (95% CI = 0.87–1.18, *n* = 173).

For the original cohort of white males employed as of August 15, 1977, SMRs rose for almost every cause of death when compared with the results of the previous study.[5] In that study, the cohort had exhibited a healthy worker effect (SMR = 0.88). The updated SMR for the original cohort was closer to one (0.97; 95% CI = 0.95–0.98) and was very close to the SMR for the expanded cohort. Similarly, the SMR for all malignant neoplasms was no longer below 1.0 (previous SMR = 0.95; 95% CI = 0.89–1.01) and at 1.07 (95% CI = 1.03–1.11) was similar to that of the expanded cohort.

The expanded cohort had a modest elevation in lung cancer mortality

TABLE 2
Summary Values for Temporal Variables by Final Portsmouth Naval Shipyard Subcohort

	Exposed Radiation Workers	Unexposed Radiation Workers	Nonmonitored Workers
No. of workers	11791	1677	24385
Year of birth (mean)	1935	1928	1932
Age first employed (mean)	28.8	30.3	30.8
Year first employed (mean)	1964	1959	1962
Year last employed (mean)	1982	1977	1972
Years employed			
Mean	18.9	18.0	10.0
Median	18.9	18.5	4.9
Percent employed at least 5 years	87.6	77.9	49.5
Years since last employed (mean)	14.0	19.7	24.2
Percent still employed as of December 31, 1996	19.4	12.5	5.6

TABLE 3
Mean Radiation Worker Monitoring Tenure by Final Cumulative Portsmouth Naval Shipyard (PNS) Dose Category

Cumulative Dose Category	No. of Workers	Tenure at PNS*	Years Monitored at PNS	Time Between Year First Employed and Year First Monitored	Percent of Tenure as Radiation Worker
0 mSv	1677	17.9	1.5	10.5	20.6
0.01–0.99 mSv	3464	16.9	3.6	8.1	37.3
1–9.99 mSv	3813	18.4	6.1	7.3	47.7
10–49.99 mSv	3032	18.8	8.7	5.6	55.6
>50 mSv	1482	24.0	14.2	6.3	64.2

* Year last employed—year first employed.

(Table 4). Excesses were seen among the nonmonitored subcohort and among exposed radiation workers. Unexposed radiation workers showed no elevation. In white females, the elevations were lower, except in exposed radiation workers, who had an SMR of 9.23 (95% CI = 1.85–30.22). However, this elevation is based on only 3 cases.

With nonmonitored workers as the baseline group, the unlagged lung cancer SRR for exposed radiation workers was 1.25 (95% CI = 0.91–1.72). The SRR for unexposed radiation workers was lower than that for the nonmonitored workforce, with an SRR of 0.79 (95% CI = 0.59–1.0).

Although each subcohort showed SMR elevations in some smoking-related causes of death (Table 4), the nonmonitored population showed elevations for every smoking-related cause of death except pancreatic cancer. In particular, point estimates were elevated with confidence intervals excluding 1.00 for emphysema and for cancers of the lung, pharynx, and esophagus. All 4 cases of esophageal cancer in women occurred in the nonmonitored cohort.

Subcohort SRR results generally followed these same patterns, with a few exceptions. In the SMR analysis, malignant neoplasms of the pancreas were as expected in the nonmonitored population but showed deficits among exposed radiation workers (SMR = 0.88; 95% CI = 0.62–1.20,

TABLE 4
Standardized Mortality Ratio (SMR) Results for Smoking-Related Causes of Death: Men and Women, All Races

	Full Cohort SMR (95% confidence interval) No. of Deaths	Exposed Radiation Workers	Unexposed Radiation Workers	Nonmonitored Workers
All causes	0.95	0.90	0.90	0.97
	(0.93–0.96)	(0.86–0.94)	(0.80–0.95)	(0.95–0.99)
	n = 12393	n = 3223	n = 638	n = 8532
All cancers	1.06	1.07	1.01	1.06
	(1.02–1.10)	(1.00–1.14)	(0.87–1.18)	(1.01–1.10)
	n = 3192	n = 950	n = 173	n = 2069
Smoking-related cancers except trachea, bronchus, and lung*	1.09	1.00	0.96	1.12
	(1.00–1.19)	(0.84–1.18)	(0.81–1.14)	(1.01–1.24)
	n = 538	n = 146	n = 33	n = 359
Trachea, bronchus, and lung	1.11	1.13	0.95	1.12
	(1.05–1.18)	(1.01–1.25)	(0.71–1.23)	(1.04–1.21)
	n = 1099	n = 356	n = 55	n = 688
Esophagus	1.36	1.34	1.70	1.35
	(1.11–1.67)	(0.90–1.92)	(0.68–3.64)	(1.03–1.74)
	n = 97	n = 30	n = 7	n = 60
Buccal cavity and pharynx	1.02	0.73	0.95	1.15
	(0.80–1.28)	(0.42–1.20)	(0.26–2.64)	(0.87–1.51)
	n = 75	n = 16	n = 4	n = 55
Pharynx	1.33	0.75	1.51	1.59
	(0.97–1.77)	(0.32–1.53)	(0.30–4.95)	(1.10–2.21)
	n = 46	n = 8	n = 3	n = 35
Larynx	1.23	0.88	1.37	1.38
	(0.90–1.64)	(0.42–1.65)	(0.28–4.49)	(0.95–1.95)
	n = 46	n = 10	n = 3	n = 33
Pancreas	0.94	0.88	0.69	0.98
	(0.79–1.10)	(0.62–1.20)	(0.25–1.58)	(0.80–1.20)
	n = 143	n = 39	n = 6	n = 98
Bladder	1.15	1.13	1.95	1.09
	(0.94–1.41)	(0.75–1.66)	(0.93–3.67)	(0.84–1.40)
	n = 100	n = 27	n = 10	n = 63
Kidney	1.07	1.09	0.73	1.10
	(0.85–1.34)	(0.70–1.63)	(0.15–2.40)	(0.81–1.45)
	n = 77	n = 24	n = 3	n = 50
Nonmalignant causes				
Chronic/unspecified bronchitis	1.14	1.15	0.50	1.20
	(0.81–1.57)	(0.55–2.16)	(0.01–4.04)	(0.80–1.74)
	n = 39	n = 10	n = 1	n = 28
Emphysema	1.08	0.84	0.91	1.19
	(0.93–1.25)	(0.59–1.16)	(0.41–1.77)	(1.00–1.42)
	n = 178	n = 37	n = 9	n = 132

* Includes malignant neoplasms of the buccal cavity and pharynx, esophagus, larynx, pancreas, bladder, and kidney.

n = 39) and unexposed radiation workers (SMR = 0.69; 95% CI = 0.25–1.58, n = 6). In contrast, in the SRR analysis, with nonmonitored workers as the baseline group (with an SRR of 1.00), the SRR for pancreatic cancer in unexposed radiation workers was elevated, at 1.57 (95% CI = 0.49–5.05). However, this result is based on only 6 cases, and the confidence interval is very wide. The results for chronic bronchitis showed a similar pattern, with the SMR for exposed radiation workers lower than that for nonmonitored workers but the SRR results reversed. The SRR for esophageal cancer for exposed radiation workers showed a smaller deficit compared with nonmonitored workers than that seen in the SMR analysis.

All cases of asbestosis and silicosis in the cohort occurred among white males. The SMR for asbestosis was highly elevated for the full cohort, with striking differences among the subcohorts (Table 5). Both monitored populations showed large elevations in asbestosis, with a more marked increase among unexposed radiation workers. In contrast, the nonmonitored population showed no excess mortality from this cause. SRR results were similar. With the nonmonitored workers as the baseline group, the SRR for exposed radiation workers was 11.25 (95% CI = 1.38–91.86, n = 7) and for unexposed radiation workers, 40.33 (95% CI = 4.49–362.06, n = 4). However, as a result of the scarcity of cases, confidence intervals are very wide and the point estimates unstable.

Malignant neoplasms in the category "other parts of the respiratory system," which encompasses cancers of the pleura, were as expected, with an SMR of 1.00 (95% CI = 0.50–1.82, n = 11). Malignant neoplasms of the peritoneum and unspecified digestive organs, which includes some cases of mesothelioma as well as a number of other causes of death, showed elevations in exposed radiation workers with an SMR of 1.15 (95% CI = 0.31–3.19) and unexposed radiation workers 2.83 (95% CI = 0.32–12.30), but a deficit among nonmonitored workers (SMR = 0.59; 95% CI = 0.19–1.47). However, the monitored subcohorts had only 4 and 2 cases, respectively.

Leukemia was the other cause of death of a priori interest. In the full cohort, leukemia mortality was as expected based on U.S. population rates (SMR = 1.01; 95% CI = 0.84–1.22, n = 115). This cause of death was in deficit in the exposed radiation workers (SMR = 0.90; 95% CI = 0.60–1.29, n = 29) and unexposed radiation workers (SMR = 0.79; 95% CI = 0.25–1.95, n = 5). Leukemia was elevated in the nonmonitored cohort, although the confidence interval includes 1.00 (SMR = 1.08; 95% CI = 0.86–1.35, n = 81).

Subcohort SRRs for leukemia were similar to SMR ratios. With the nonmonitored group used as the baseline, the SRR for unexposed radiation workers was 0.59 (95% CI = 0.24–1.46, n = 5) and for exposed radiation workers, 0.81 (95% CI = 0.47–1.38, n = 29). Anemia of other/unspecified types (nonpernicious) also showed the greatest elevation in the nonmonitored cohort with an SMR of 1.42 (95% CI = 0.79–2.37), although point estimates were elevated among white males in all subcohorts. Only 2 cases of anemias of these types were seen in white females, both in the nonmonitored group, for an SMR of 1.90 (95% CI = 0.21–8.25).

The SMR for malignant neoplasms of the liver, unspecified type, was elevated in the full cohort (SMR = 1.39; 95% CI = 0.94–1.97, n = 31). This category includes malignant liver neoplasms, which have not been determined to be primary or metastatic. In contrast, the category malignant neoplasms of the biliary passages, liver, and gallbladder showed deficits across the cohort (full cohort SMR = 0.85; 95% CI = 0.61–1.14, n = 43), as did cirrhosis and alcoholism. Malignant neoplasms of other/unspecified sites were elevated across the cohort (SMR = 1.25; 95% CI = 1.10–1.42, n = 241).

Finally, several less common neoplasms, not of a priori interest, showed elevations, but cases were scarce and confidence intervals wide. In the full cohort, malignant neoplasms of the thyroid had an SMR of 1.25 (95% CI = 0.50–2.68, n = 7), but the only subcohort showing an excess was exposed radiation workers, with 4 cases and an SMR of 2.66

TABLE 5
Standardized Mortality Ratio (SMR) Results: Asbestosis and Silicosis in Men and Women, All Races (based on 1960–1999 rates)

	Full Cohort SMR (95% confidence interval) No. of Deaths	Exposed Radiation Workers	Unexposed Radiation Workers	Nonmonitored Workers
Asbestosis	5.71	10.02	30.14	0.79
	(2.95–10.16)	(4.01–21.46)	(8.11–83.63)	(0.01–6.42)
	n = 12	n = 7	n = 4	n = 1
Silicosis	1.12	1.47	n = 0	1.09
	(0.22–3.66)	(0.02–12.01)		(0.12–4.72)
	n = 3	n = 1		n = 2

(95% CI = 0.72–7.39). Only 1 of these 4 cases occurred in an employee with a cumulative exposure above 3 mSv. Malignant neoplasms of the eye were elevated with 4 cases (SMR = 1.86; 95% CI = 0.50–5.17). The category "neoplasms of unspecified nature of the eye, brain, and other parts of the nervous system, unspecified" was elevated with 23 cases (SMR = 1.46; 95% CI = 0.92–2.20). Larger excesses were seen among exposed radiation workers and nonmonitored workers than in unexposed radiation workers.

Differences between long-term workers and all workers (of any tenure) within each subcohort were examined to see whether the shorter average tenure of nonmonitored workers was responsible for differences between the subcohorts. In analyses restricted to workers employed at least 5 years, the overall SMR was 0.96 (95% CI = 0.94–0.98) and the all-cancer SMR was again elevated at 1.07 (95% CI = 1.03–1.11). Within each subcohort, mortality from smoking-related causes of death failed to show consistent patterns suggestive of marked differences in tobacco consumption between short- and long-term workers; SMRs for some smoking-related causes rose, whereas others declined when analyses were restricted to longer-term workers. The full cohort and subcohort lung cancer SMRs were almost unchanged with the minimum employment restriction.

Combined Maine and New Hampshire Comparison Population

The all-cause SMR for the combined Maine and New Hampshire comparison population was slightly lower than the SMR for the U.S population when rates from 1960 forward are used (the rates available for Maine and New Hampshire). The full-cohort SMR was 0.94 using Maine–New Hampshire rates and 0.96 using U.S. population rates. However, all-cancer mortality, which was elevated compared with the U.S. population, was as expected compared with the combined Maine–New Hampshire population.

The SMRs for most smoking-related causes of death were also lower when the combined Maine–New Hampshire mortality rates were used for comparison. The SMR for asbestosis in the full cohort was lower using the state rates (3.90; 95% CI = 2.01–6.93), but the SMR for silicosis was higher (1.64; 95% CI = 0.33–5.38). SMRs were slightly higher for leukemia (1.09; 95% CI = 0.89–1.31) but lower for anemia of other/unspecified types (1.21; 95% CI = 0.74–1.89). The decreased stability of point estimates using this smaller comparison group must be kept in mind.

Differences among the subcohorts were similar to those seen in the U.S population analyses (data not shown). The nonmonitored subcohort again had the highest all-cause SMR, just below the comparison population at 0.97 (95% CI = 0.95–0.99).

Dose Analyses

To explore elevations for specific causes of death seen in monitored workers, SRRs were calculated stratifying on cumulative external dose, using categories of 0–<1, 1–<10, 10–<50, and >50 mSv. SRRs were calculated for leukemia using 0-, 2-, and 5-year lags. In the 2-year lagged analysis, which produced the strongest dose-response relation for leukemia, the SRRs rose monotonically with increasing dose (Table 6). The corresponding SMRs were in deficit for the comparison category and for the 1–<10-mSv group, with elevations in the 2 higher dose groups much more modest than those seen in the SRR (10–<50 mSv SMR = 1.46; >50 mSv SMR = 1.57). In contrast, all 6 cases of anemia of other and unspecified types in badged workers occurred among workers in the first 2 dose categories.

We examined SRRs for lung cancer with 0-, 10-, 15-, and 20-year lag periods. The highest SRR was observed with the 15-year lag. Lung cancer showed elevations for the 1–<10-mSv and 10–<50-mSv categories compared with the baseline group, but almost no increase in workers with at least 50-mSv cumulative dose (Table 7). We also applied a 15-year lag to analyses of other smoking-related causes of death. Emphysema and cancers of the esophagus, pancreas, and bladder exhibited inverse dose-response relations, with a statistically significant trend for emphysema. Cancers of the larynx, pharynx, and kidney showed positive dose-responses, but none of the trends was statistically significant.

We examined 10- (data not shown), 20-, and 30-year lagged analyses for asbestosis. The choice of lag strongly influenced the dose-response for this outcome. Although a 20-year lag yielded a negative slope and similar SMR values for each dose category, a 30-year lag gave a positive slope and much larger SMRs for the 2 dose groups in which deaths occurred (1–<10 mSv and >50 mSv) than in the baseline zero-dose group (Table 8). No cases remained in the intermediate exposure category, 10–<50 mSv, once the 30-year lag was applied. The Rothman test for linear trend was not significant with either lag period.

When prior dose was added to dose received at the shipyard, we saw little change in the exposure-response relations for leukemia, lung cancer, and other causes of death. In general, SRRs for the higher dose categories diminished slightly, with small decreases in the slope.

Discussion

The results of this study suggest that monitored and nonmonitored PNS workers had very different occupational and nonoccupational exposure histories. In the expanded cohort, monitored workers exhibit a strong healthy worker effort, whereas their nonmonitored col-

TABLE 6
Dose-Response Results: Leukemia in Men and Women, All Races, 2-Year Lag

Dose Category	0–<1 mSv	1–<10 mSv	10–<50 mSv	>50 mSv	Slope† and Standard Error (SE)
SRR (95% CI)	1.00	2.05 (0.77–5.47)	2.98 (1.12–7.97)	5.13 (1.37–19.19)	Slope: 3.38e–06
No. of deaths	7	10	10	7	SE: 1.03e–06*
SMR (95% CI)	0.46 (0.18–0.99)	0.90 (0.43–1.70)	1.46 (0.70–2.74)	1.57 (0.63–3.38)	

* Two-sided *P* value <0.01.
† Standardized rate per person-year—mSv.
SRR, standardized rate ratio; CI, confidence interval; SMR, standardized mortality ratio.

TABLE 7
Standardized Rate Ratios (SRRs) for Smoking-Related Causes, Portsmouth Naval Shipyard Dose, Males and Females, All Races, 15-Year Lags

Dose Category: Cause of Death	0–<1 mSv SRR 95% CI No. of Deaths	1–<10 mSv	10–<50 mSv	>50 mSv	Rothman Trend Test: Slope† and Standard Error (SE)
Malignancies					
Trachea, bronchus, and lung	1.00	1.30 (0.90–1.88)	1.35 (0.97–1.89)	1.04 (0.69–1.56)	Slope: 5.10e–07 SE: 4.24e–06
	n = 108	n = 97	n = 72	n = 39	
Esophagus	1.00	0.45 (0.19–1.08)	0.22 (0.05–0.94)	0.25 (0.06–1.09)	Slope: −1.02e–06 SE: 9.18e–07
	n = 20	n = 7	n = 2	n = 2	
Larynx	1.00	0.56 (0.10–3.10)	1.90 (0.40–8.91)		Slope: 1.14e–06 SE: 1.55e–06
	n = 4	n = 2	n = 3	n = 0	
Pharynx	1.00	0.67 (0.13–3.58)	1.32 (0.24–7.20)		Slope: 4.27e–07 SE: 8.61e–07
	n = 5	n = 2	n = 2	n = 0	
Pancreas	1.00	1.64 (0.71–3.78)	0.99 (0.34–2.92)	1.05 (0.33–3.30)	Slope: −1.91e–07 SE: 6.08e–07
	n = 11	n = 13	n = 5	n = 5	
Kidney	1.00	2.00 (0.65–6.17)	1.66 (0.45–6.19)	2.54 (0.68–9.54)	Slope: 8.51e–07 SE: 5.99e–07
	n = 5	n = 8	n = 4	n = 4	
Bladder/other urinary organs	1.00	0.43 (0.15–1.18)	0.56 (0.19–1.69)	0.39 (0.09–1.71)	Slope: −4.89e–07 SE: 6.81e–07
	n = 16	n = 5	n = 43	n = 2	
Nonmalignant causes					
Chronic bronchitis	1.00	2.60 (0.48–14.22)		1.47 (0.13–16.27)	Slope: 5.68e–08 SE: 4.12e–07
	n = 2	n = 4	n = 0	n = 2	
Emphysema	1.00	0.49 (0.11–2.30)	0.21 (0.04–1.20)	0.11 (0.01–1.25)	Slope: −1.72e–06* SE: 7.51e–07
	n = 12	n = 14	n = 4	n = 1	

* Two-sided *P* value <0.05.
† Standardized rate per person-year—mSv.

leagues do not. Mortality from several specific causes of death also differs greatly by subcohort. Previous studies of PNS workers[5] had similar findings, which have been attributed to differences in environmental/lifestyle exposures such as smoking.[13] The excess of deaths among nonmonitored workers is consistent with increased smoking among this subcohort. At the same time, findings of strongly elevated risks for asbestosis among monitored workers and a deficit of deaths from this cause among nonmonitored workers suggest that other occupational exposures are also not randomly distributed with respect to occupational radiation exposure and require further investigation.

The average employment duration differed substantially among the subcohorts, which could explain some of the contrasting mortality findings.

TABLE 8
Dose-Response Results: Asbestosis in Men and Women, All Races (based on 1960–1999 rates), 10, 20, and 30-Year Lag Periods

Lag Period	0–<1 mSv	1–<10 mSv	10–<50 mSv	>50 mSv	Slope* and Standard Error (SE)
10 year					
SRR (95% CI)	1.00	0.71 (0.17–2.98)	0.75 (0.14–3.87)	0.38 (0.04–3.29)	Slope: −3.15e–07
No. of deaths	5	3	2	1	SE: 1.04e–07†
SMR	17.50	13.29	14.40	10.27	
20 year					
SRR (95% CI)	1.00	0.78 (0.17–3.52)	0.82 (0.15–4.49)	0.48 (0.05–4.35)	Slope: −2.46e–07
No. of deaths	4	3	2	1	SE: 7.99e–08†
SMR	16.01	15.80	17.21	13.51	
30 years					
SRR (95% CI)	1.00	2.59 (0.42–15.94)	0	6.44 (0.58–71.07)	Slope: 1.64e–06
No. of deaths	2	3	0	1	SE: 1.15e–06
SMR	12.49	35.83	0	50.23	

* Standardized rate per person-year—mSv.
† Two-sided *P* value <0.01.
SRR, standardized rate ratio; CI, confidence interval; SMR, standardized mortality ratio.

Although the 2 larger cohorts, exposed radiation workers and nonmonitored workers, are quite similar with respect to birth cohort, age first employed, and year of first employment, they exhibit striking differences in duration of employment (and therefore in year last employed and time since last employed).

A number of studies have observed differences in mortality outcomes for short-term versus long-term employees.[14–19] The nonmonitored workers had a much shorter average duration of employment, with fewer than half employed as long as 5 years. Interestingly, limiting SMR analyses to workers employed for at least 5 years led to small changes in SMRs for smoking-related cancers but did not change the pattern of between-subcohort SMR differences for these outcomes. These findings suggest that between-cohort mortality differences are more the result of lifestyle differences than a healthy worker survivor effect,[20–22] and that these lifestyle differences are greater between subcohorts than between long- and short-term workers within each subcohort.

Within a cohort, for a secondary exposure to confound the relation between a primary exposure and the outcome of interest, the distribution of the secondary exposure must be nonrandom with respect to the distribution of the main exposure of interest. Petersen et al.[23] examined the relation between external radiation exposure and tobacco use among workers monitored for external exposure at least 3 years at the U.S. Department of Energy Hanford facility. The researchers found no strong relationship between tobacco use and cumulative radiation dose equivalent, and no association at all when adjusting for year of birth.

In contrast, examination of SMR results for PNS subcohorts suggests that in this workforce, smoking habits or some related lifestyle factor could have differed by radiation monitoring status. Nonmonitored workers had excess mortality from every smoking-related cause of death except pancreatic cancer. Some of these smoking-related causes were in excess among radiation workers as well; the point estimates for esophageal cancer were elevated in every subcohort, and point estimates for malignancies of the pharynx and larynx were elevated in unexposed radiation workers. However, the SRRs for esophageal cancer, as well as for emphysema, exhibited inverse dose-responses with radiation exposure in lagged analyses, suggesting that excesses observed for some of these outcomes could be related to differential distribution of smoking even within the monitored workforce or to other occupational exposures. Among exposed workers, those with lower cumulative doses spent less time as radiation workers and spent more years at the site before becoming radiation workers, on average, than did their counterparts with higher cumulative dose. Thus, they could have shared exposure characteristics of nonmonitored workers for longer portions of their tenure at the site.

Also suggestive of a nondifferential distribution of a potential confounding exposure is the large excess of asbestosis observed only among monitored workers. Although the SMR is more highly elevated in workers with zero recorded radiation dose than in exposed radiation workers, when a 30-year lag is applied to the analysis of asbestosis, SRRs for the 2 positive dose categories that retain cases are much higher than that of the baseline group. This suggests that the observation of a higher asbestosis SMR in unexposed than in exposed radiation workers could be an artifact resulting from the earlier and long employment of the unexposed radiation workers, many of whom were engaged in radiation

work when stringent protective procedures for asbestos work had not yet been implemented.

These findings suggest that differences in mortality patterns between monitored and nonmonitored workers could be facility-specific. Specific aspects of radiation work at PNS could have contributed to a differential distribution of smoking within this cohort. Much of the work necessitating radiation qualification was carried out on the submarines, where restrictions on smoking could have been stronger than throughout the rest of the site, so heavy smokers might have been reluctant to apply for radiation work. Other selection or retention factors probably pertain to Department of Energy or Atomic Weapons Establishment sites. The additional medical examination required for radiation qualification at PNS could have added a second level of healthy worker selection.

The excess of several smoking-related cancers (esophagus, larynx, pharynx, and bladder) among unexposed radiation workers approached that seen in nonmonitored workers. However, the deficits observed for emphysema and chronic bronchitis among unexposed radiation workers suggest that smoking alone is unlikely to explain the cancer elevations among these workers. Nonradiologic occupational exposures could be involved, with asbestos 1 obvious candidate.

Like in the previous cohort study, no overall excess of leukemia mortality was observed. In SMR analyses, excess leukemia deaths were seen only in the nonmonitored subcohort. However, internal analyses of monitored workers showed elevations at exposures of 1 mSv or more, with a significant, positive linear dose-response. These results suggest the need for further investigation of the relation between radiation and leukemia in monitored workers, including assessment of the role of solvent exposure as a potential confounder.

The lower overall mortality among PNS radiation workers in the higher-dose categories, compared with those with less cumulative exposure, has been used recently to argue that low-level radiation exposure is beneficial to health.[24] The present analysis suggests that confounding by factors such as selection of healthier workers for radiation work, lifestyle differences, and perhaps exposure of nonmonitored workers to other workplace hazards is responsible for the apparent mortality deficit among the radiation-exposed workers. Many of these potential sources of bias are being addressed in nested case-control studies and statistical modeling of this population of workers. Further analyses of this and other nuclear worker cohorts should consider carefully the most relevant comparison group for highly exposed radiation workers and should use appropriate study methods to adjust for likely confounding factors to minimize these sources of bias.

Limitations

Workers of unknown vital status were assumed to be alive, a decision which would cause downward bias of the SMRs. To assess the magnitude of this potential bias, we reran all analyses using the date last observed instead of the end-of-study date to truncate follow up for workers of unknown vital status. Most person-years lost under this modification come from the nonmonitored cohort. Therefore, the increase in SMRs when DLO is used in place of end of study is much more marked in this subcohort than among radiation workers. However, the differences in all analyses were small and did not alter conclusions about the mortality patterns in the full cohort or in any subcohort.

Underascertainment of cause of death is an also issue in this cohort. Death certificates were missing for 1.7% of deceased workers. Ascertainment of cause of death, particularly for malignant neoplasms, seems to have been less specific in the PNS cohort than in the general U.S. population, as reflected by excesses in the residual category of neoplasms. Most of these deaths were the result of malignant neoplasms for which the primary site was not determined. The SMR for malignant neoplasms of the liver, which could not be designated as either primary or secondary, was also elevated. Because cirrhosis of the liver and alcoholism showed deficits across the cohort, alcohol is unlikely to be responsible for the excess unspecified liver cancer deaths. Instead, ascertainment of primary sites of malignancies appears to be poor in this population. If primary sites of these fatal malignancies were known, SMRs for the corresponding cancer outcomes would be higher.

Subcohort misclassification is a potential problem as a result of the failure to record zero dose between 1962 and 1964, higher detection limits in the earlier years, and any failures to transfer dose to electronic files. These factors could have led some workers with positive or zero cumulative dose to be assigned to the nonmonitored subcategory and some workers with positive dose to the unexposed radiation worker subcohort. Including monitored workers in the nonmonitored group should only attenuate any actual differences between the subcohorts. The striking contrasts that remain suggest that misclassification is limited and that differences between the groups are robust.

Within the monitored subcohorts, missed dose as described here could lead to misclassification of exposed workers into lower cumulative dose categories than where they belong and thus to a flattening of any linear dose-response that might exist. However, reviews of subsets of the dosimetry data for the original[5] and expanded cohorts[6a] found that the dose-transfer error rate was very low ($<1\%$).

Missing information on prior exposures is another potential limitation. However, with available data,

adding prior dose to the shipyard dose produced very little change in the results. The absence of a larger effect is probably the result of the small contribution of prior dose compared with the cumulative shipyard dose. Unless a large proportion of prior dose remains unaccounted for, this type of missed dose is unlikely to create a substantial bias.

Conclusions

The healthy worker effort seen in the 1980 evaluation of white males employed at PNS as of August 15, 1977, has diminished with additional follow up, but overall mortality for the expanded cohort was still slightly less than that expected from U.S. population rates. Mortality rates from a number of nonmalignant causes, including disease of the heart, circulatory system, and digestive system, were below expectation. Cancer death rates, however, were slightly higher than expected.

Although the overall SMR for leukemia was as expected, the point estimates for leukemia mortality were elevated among both nonmonitored workers and radiation workers with cumulative exposures above 10 mSv. The observation of a positive dose-response relation between external radiation exposure and leukemia is consistent with the conclusions of a recent review of studies of leukemia in nuclear workers,[25] which collectively suggests a slight positive dose-response for subtypes other than chronic lymphocytic leukemia, the radiogenicity of which is the subject of ongoing debate. The rate ratios observed in the dose categories used for the PNS cohort are somewhat higher than observed in other cohorts[26]; however, confidence intervals are very wide. In addition, solvent exposure is an important potential confounder that could not be addressed in the full cohort analyses.

Lung cancer was elevated, although not significantly, among workers with exposures between 1 and <50 mSv, but not in the most highly exposed group (>50 mSv). The deficit of emphysema in this group suggests that these elevations are unlikely to be inflated to any great degree by smoking. However, any definitive claim about the distribution of smoking and occupational radiation exposure and the role of smoking in excess cancer mortality observed in this cohort requires systematic assessment of individual-level smoking data for the workers.

One of the most striking findings of this study was the contrast between very high excess of asbestosis in monitored workers and the absence of any elevation among nonmonitored workers. These findings suggest that exposures to asbestos and nuclear work are not independent at this facility. This observation likely reflects higher exposures incurred in enclosed spaces, because radiation workers were more likely to be working shipboard than their nonmonitored counterparts.

In the previous lung cancer case-control study at PNS,[3] the apparent relation between external ionizing radiation and lung cancer was attenuated after controlling for exposures to asbestos and welding fume. This finding, together with the observation of increased asbestosis mortality among workers with higher cumulative external dose (with a 30-year lag) in this cohort update, suggests that asbestos exposure is likely to explain at least part of the observed lung cancer excess among radiation workers in this cohort. Although no mortality outcome specifically implicates welding fume, the findings of the previous study highlight the potential role of this exposure in the observed lung cancer excess.

Several NIOSH studies currently underway are designed to examine more closely the relations between external radiation exposure and specific causes of death while assessing the role of coexposures such as asbestos and welding fume in the lung cancer findings and solvents in the leukemia results. A modeling phase of the cohort study is using job and shop titles (available for monitored workers during years in which they were radiation-monitored), combined with professional judgment, to develop categorical assignments for these coexposures for Poisson regression analyses. A nested case-control study of leukemia is assessing the role of solvent exposures and will incorporate occupational medical x-ray exposures. Finally, a lung cancer case-control study is using individual smoking data when available and individual and area monitoring data for asbestos and welding fume to examine how these coexposures affect the relation between lung cancer and external radiation exposure in PNS workers. Collectively, these additional studies should facilitate greater understanding of the causes of excess mortality observed in this cohort evaluation.

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