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Summary of Retrospective Asbestos and Welding Fume Exposure Estimates for a Nuclear Naval Shipyard and Their Correlation with Radiation Exposure Estimates

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In support of a nested case-control study at a U.S. naval shipyard, the results of the reconstruction of historical exposures were summarized, and an analysis was undertaken to determine the impact of historical exposures to potential chemical confounders. The nested case-control study (N = 4388) primarily assessed the relationship between lung cancer and external ionizing radiation. Chemical confounders considered important were asbestos and welding fume (as iron oxide fume), and the chromium and nickel content of welding fume. Exposures to the potential confounders were estimated by an expert panel based on a set of quantitatively defined categories of exposure. Distributions of the estimated exposures and trends in exposures over time were examined for the study population. Scatter plots and Spearman rank correlation coefficients were used to assess the degree of association between the estimates of exposure to asbestos, welding fume, and ionizing radiation. Correlation coefficients were calculated separately for 0-, 15-, 20-, and 25-year time-lagged cumulative exposures, total radiation dose (which included medical X-ray dose) and occupational radiation dose. Exposed workers' estimated cumulative exposures to asbestos ranged from 0.01 fiber-days/cm³ to just under 20,000 fiber-days/cm³, with a median of 29.0 fiber-days/cm³. Estimated cumulative exposures to welding fume ranged from 0.16 mg-days/m³ to just over 30,000 mg-days/m³, with a median of 603 mg-days/m³. Spearman correlation coefficients between cumulative radiation dose and cumulative asbestos exposures ranged from 0.09 (occupational dose) to 0.47 (total radiation dose), and those between radiation and welding fume from 0.14 to 0.47. The estimates of relative risk for ionizing radiation and lung cancer were unchanged when lowest and highest estimates of asbestos and welding fume were considered. These results suggest a fairly large proportion of study population workers were exposed to asbestos and welding fume, that the absolute level of confounding exposure did not affect the risk estimates, and that weak relationships existed between monitored lifetime cumulative occupational radiation dose and asbestos or welding fume.

Keywords confounding, exposure assessment, lung cancer

INTRODUCTION

A 1970s study by Najarian⁽¹⁾ at the Portsmouth Naval Shipyard (PNS) found an excess of all cancers combined. Since then, the National Institute for Occupational Safety and Health (NIOSH) has been studying the shipyard in an effort to clarify the relationship between ionizing radiation exposure at the shipyard and mortality from various diseases.

In their initial cohort mortality study, NIOSH found a dose-response effect between lung cancer and ionizing radiation. This effect was reduced in a nested case-control analysis of the same population that controlled for welding fume and asbestos.⁽²⁾ NIOSH updated the original cohort study at the shipyard in the 1990s^(3,4) and recently completed nested case-control studies of leukemia⁽⁵⁾ and lung cancer.⁽⁶⁾ The latter nested case-control study of lung cancer and ionizing radiation evaluated the relationship between external ionizing radiation and lung cancer while adjusting for the potential confounders gender, radiation monitoring status, smoking habit surrogates (socioeconomic status and birth cohort), and exposures to welding fumes and asbestos.

This article summarizes the results of the reconstruction of historical exposures (other than radiation) on which the lung cancer nested case-control study was based; to examine the potential for confounding by determining the degree to which cumulative exposures to ionizing radiation and the potential confounders/effect modifiers are correlated; and to determine whether the risk estimates found in the NIOSH 2006 nested case control study remain unchanged over the estimated range of exposures to the confounders.

Additional potential exposures discussed here, chromium and nickel (in welding fume), were not included in the case-control analysis due to estimated exposure to a very limited proportion of the population. Welding fume and, in particular,

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the chromium and nickel components have been identified as possible causes of lung cancer in previous epidemiology studies.⁽⁷⁾ In 1990, the International Agency for Research on Cancer (IARC) concluded that welding fumes were “possibly carcinogenic” to humans, based on limited evidence in humans and inadequate evidence in animals.⁽⁸⁾

Description of Shipyard

Portsmouth Naval Shipyard is located in Kittery, Maine, was originally established as the first U.S. Navy shipyard in 1800 and, at the time, had about 50 employees. Employment peaked during and immediately following World War II, at about 20,000. The shipyard built its first nuclear submarine in 1958 and its last one in 1969. After 1971, the shipyard switched entirely to overhaul, repair, and refueling of nuclear-powered submarines. Employment has shrunk over the years, but as of 2002, it was nearly 4000.

PNS is a large industrial complex where hundreds of tasks are performed both in buildings and on ships and are organized into “shops.” A shop consists of a group of related and unrelated trades working on some component of ships, such as pipe or woodworking, or in a shipyard support function, such as the supply shop and the power plant. A shop may be located in a single building or, more likely, in several locations in the shipyard, and trades might work primarily in buildings, aboard ships, or both. Tasks include cutting and welding steel hull sections; wood, rubber, and plastic fabrication and installation; foundry operations; automotive repair; shipfitting and rigging; electrical and electronics repair and installation; pipefitting; painting and paint removal. There are also engineering, health and safety, administrative, personnel, and other support functions. Specific job titles may exist in only one shop or, in some cases, may exist in two or more shops.

Description of Hazards and Monitoring Data

Historically, asbestos exposure was present in many jobs in the pipefitting, plumbing, woodworking, shipfitting, transportation, welding, and electrical shops. Asbestos was ubiquitously used as pipe and boiler insulation on submarines; therefore, additional jobs that were primarily conducted shipboard were also exposed to asbestos. Until the 1960s, the U.S. Navy used chrysotile and amosite asbestos insulation on naval vessels to insulate pipes, boilers, and machinery.⁽⁹⁾

In the mid-1970s the process of removing asbestos insulation from ships began and was ongoing until the 1990s. Exposures to chromium and nickel in welding fumes occurred primarily after the initiation of nuclear submarine construction in 1953, which involved increased use of stainless steel containing these metals.

A NIOSH database of PNS air sampling survey reports identified 58 unique contaminants monitored by shipyard personnel from 1943 to 1994, comprising 4714 sample results. These were primarily area samples not linked to a specific shop or job title but usually described a process or sampling location within the shipyard or on board a ship. The database contains

1754 asbestos samples that were measured by several different methods, including konimeter, impinger, and membrane filter. Asbestos full-shift, or near full-shift (greater than 6 hr, N = 915) samples ranged from 0.004 fibers/cm³ to 25 fibers/cm³. Welding fume, chromium, and nickel were only occasionally sampled over the years at the shipyard.

METHODS

Summary of Estimation Methods

The following is a brief summary of the methodology used to reconstruct asbestos and welding fume exposures at the shipyard. A separate, previously published paper details the methodology used to reconstruct the historical exposures.⁽¹⁰⁾ Radiation exposure estimates for this population also have been previously summarized.⁽¹¹⁾

Shipyard monitoring data were not considered useful as a basis for either a direct exposure reconstruction or for a validation of exposure estimates. Air sampling data were rarely associated with job titles and were not well distributed over the period of the study (1945–1996). Although identified more often in the sampling records, “shop” was not considered a useful grouping mechanism, as it did not necessarily identify the location of the sampling, the job title, or personnel involved, nor the process or task.

Although large numbers of measurements were made in some shops, such as woodworking, maintenance, and pipe, most shops were the subject of few or no measurements. In addition, most monitoring at the shipyard was either complaint or compliance based. Air monitoring data for hazards other than asbestos, such as welding fumes, were even more sparse and incomplete. Therefore, it was necessary to find an alternate exposure reconstruction approach.

An expert panel, consisting of three industrial hygienists intimately familiar with exposures at the shipyard, estimated exposures to asbestos and welding fumes at PNS.⁽¹⁰⁾ Original shops and job titles were standardized by NIOSH and compiled into a job exposure matrix consisting of 3519 standardized shops, standardized job titles, and 3-year time periods. Increments of 3 years were used to construct the job exposure matrix to reduce the number of estimates needed by the panel and still retain reasonable resolution of estimates over time.

A small subset (N = 915) of shipyard-generated asbestos personal and area monitoring data was used to define the range of potential asbestos exposures at the shipyard and to quantify exposure categories. To more accurately represent worker exposures, the criteria for selecting measurement data for this purpose included: (1) samples greater than 6 hr in duration; (2) samples after membrane filter sampling and phase-contrast microscopic analyses were adopted (after 1970); and (3) excluding clearance measurements, almost all of the results of which were below the limit of detection, and none of which represented actual worker exposures.

Four categories were set, based on quartiles calculated from cumulative frequency plots, which were used as category

boundaries. Arithmetic means of the sampling data within each quartile were chosen as the asbestos exposure intensities. A fifth category of "background" was chosen based on the mean of ambient air sample results and judgment derived from existing documents describing asbestos control in various periods at the shipyard. The five categories were: (1) background (0.004 f/cm^3 until 1978 or 0.002 f/cm^3 during and after 1978); (2) very low (0.03 f/cm^3); (3) low (0.75 f/cm^3); (4) medium (1.85 f/cm^3); and (5) high (8.09 f/cm^3). Prior to beginning their assessments of exposures, the expert panel members were asked to review these categories and they confirmed these were appropriate to cover all periods at the shipyard.

Due to the paucity of shipyard monitoring data, consensus guidelines (ACGIH's[®] threshold limit values [TLVs[®]]),⁽¹²⁾ or NIOSH recommended exposure limits [RELS]⁽¹³⁾ for nickel) were used to quantitatively specify three exposure categories for each of welding fume, chromium, and nickel. For welding fume, values were assigned of background (0.025 mg/m^3); low (2.5 mg/m^3); and high 10 mg/m^3). Nonzero background exposures were assumed for asbestos and welding fume because of widespread presence in the shipyard.

For chromium, values were assigned of background ($0 \text{ } \mu\text{g/m}^3$); low ($4.9 \text{ } \mu\text{g/m}^3$); and high ($20 \text{ } \mu\text{g/m}^3$). Comparable values for nickel were background ($0 \text{ } \mu\text{g/m}^3$), low ($9.0 \text{ } \mu\text{g/m}^3$), and high ($40 \text{ } \mu\text{g/m}^3$). Values of zero were assigned for background exposure to chromium and nickel because exposure to these agents was not nearly as widespread at the shipyard.

In addition to exposure intensity (8-hr TWA), the panelists estimated a range of intensity of exposure (lowest and highest) over which most of the workers in that shop/job/time period combination would be exposed, frequency of exposure (days per year exposed at the estimated intensity), and for asbestos only, respirator use and type. The range chosen by each panelist could be the same as the chosen best intensity, but it often was different. It was almost always the same for shop/job title/time period combinations that were judged to be unexposed (background intensity). However, the panelists were free to choose the value for all three (best, low, and high) intensity estimates.

Job dictionaries, detailed instructions, and examples of how to fill in cells and four blank job exposure matrices (one for each contaminant) were given to the expert panel members. Each of the three panelists, blinded to the others, provided their estimates of intensity, frequency, highest and lowest exposure, respirator use, and respirator type for each of the 3519 standardized shop/job title/3-year time period combinations (cells) in the exposure matrices.

Because the exposure estimation process amounted to considerable work on the part of the panelists, they were given a suggested timeline but were allowed as long as they needed to complete the estimates. The panelists' estimates were returned to the authors within 2 to 3 months from the time they received them. After each panelist submitted his initial estimates, final estimates were generated through a

series of consensus meetings in which each discordant cell was discussed by all three panelists.

The percent concordances of intensity estimates (defined as differing by no more than one exposure category) were quite good: 77.9% for welding fume, 90.6% for asbestos, and 99.3% for chromium and nickel. Percent concordances of exposure frequency estimates ranged from 96% to 99%. Pairwise kappa statistics comparing annual exposure estimates indicated higher agreement between two of the three panelists (Panelists 2 and 3, 0.49–0.56) than between those two panelists and the third (Panelist 1, 0.07–0.44).⁽¹⁰⁾ This was resolved during the follow-up consensus meetings, during which it was discovered Panelist 1 had misunderstood some of the instructions. An extensive description of this process, and an evaluation of the panel estimates, including the levels of inter-rater agreement, has previously been published.⁽¹⁰⁾

Calculation of Annual Exposures

Annual exposure estimates for each cell of the four exposure matrices were calculated from the final intensity, frequency, and, in the case of asbestos, respirator use and type.⁽¹⁰⁾ For each shop/job-title/3-year time period combination, annual exposure equaled the product of intensity and frequency. Intensities were expressed in units of fibers/cm³ for asbestos, mg/m³ for welding fume and $\mu\text{g/m}^3$ for nickel and chromium. Frequency values ranged from 0–240 days (weekends and holidays were not included) of exposure per year. In the case of asbestos, if respirators were required the product of intensity and frequency was divided by a designated assigned protection factor (APF) based on the type of respirator.⁽¹⁴⁾

To account for background exposures for unexposed days, the frequency was subtracted from 240 and multiplied by the background exposure level for that contaminant. This product was then added to that cell's annual exposure. The estimates were quantified in terms of annual cumulative exposure (for example, cumulative annual asbestos exposure in terms of fiber-days/cm³) for each shop/job title/3-year time period.

To examine trends in estimated exposures over time, the shop/job annual cumulative exposures were used to calculate geometric means for each 3-year time period from 1945–1995. The geometric means were computed separately for several different groups of exposed standardized jobs (e.g., the geometric mean for the combined medium and high asbestos-exposed jobs in each time period and for the combined very low and low asbestos-exposed jobs in each time period) and for all standardized jobs held by workers within the study population in each time period. These time-period-specific geometric mean exposures for exposed jobs, all jobs, and the estimated annual exposures for specific jobs were graphed to visually determine whether there were any trends in exposure over time among the exposed jobs or among all jobs.

Calculation of Workers' Cumulative Exposures

The estimates of exposures by shop, job title, and time-period were used in conjunction with each worker's employment history (N = 4388) to compute all workers'

estimated cumulative exposures. Cumulative exposure is the sum of the exposures in all of the jobs held by an individual worker over that person's working lifetime, weighted by the time spent in each job. The annual exposure for each shop/job title/time period combination was first converted into a daily exposure. Using each worker's employment history, daily exposures were summed over that worker's career at the shipyard. Cumulative exposure was measured in units of fiber-days/cm³ for asbestos, mg-days/m³ for welding fumes, and μ g-days/m³ for chromium and nickel.

To provide a frame of reference for the lifetime cumulative exposures, two procedures were followed. First, cumulative exposure estimates were compared to recognized exposure guidelines (2005 ACGIH TLV values)⁽¹²⁾ accumulated over time periods of 1 and 10 years, assuming 240 exposed working days in a year. A TLV-1 is equivalent to an exposure at the TLV for 240 working days per year, and a TLV-10 would be that value multiplied by 10. For example, the asbestos TLV-10 would be 240 fiber-days/cm³ (0.1 f/cm³ * 240 working days/year * 10 years).

Although any number of years could be used, 1-year and 10-year TLVs were used as a point of comparison in these analyses. In the epidemiology analyses, models were run using categories surrounding the TLV-10 (asbestos) and TLV-1 (welding fume) because they reflected current knowledge regarding the toxicology of asbestos and welding fume and allowed the setting of reasonable cut points within this study population.

The second frame of reference to judge cumulative exposures was calculated by multiplying the TLV or REL (in the case of nickel) by each worker's duration of exposure in days. The percentage of workers whose cumulative estimated exposure exceeded this "cumulative TLV/REL" (hereafter referred to as the cumulative TLV) was calculated for each of the four hazards. This was done separately for all workers combined and exposed-only workers.

STATISTICAL ANALYSIS

Distributions of cumulative exposure estimates of all workers were examined to assess the proportions of the study population exposed to various cumulative exposures, to assess the percentages of the population overexposed over time periods of greater than a year, and to assist in determining appropriate cut points for dose-response analyses.

Examination of frequency histograms and quantile-quantile charts (Q-Q charts, not shown) indicated that the estimated data distributions (with the possible exception of nickel) approached lognormal but, because of the large sample size, were statistically different from lognormal. Scattergrams comparing the cumulative exposure estimates also indicated a substantial departure from linearity. Due to the uncertainty about the underlying true distributions and the nonlinearity,

nonparametric statistics were calculated to test and examine the degree of association between exposures. In addition, both arithmetic means and medians are summarized in the tables.

Characteristics of the associations between all of the exposure variables were examined using scatter plots. The initial results indicated that some exposure variables were correlated, but both original and log-transformed exposure score scatter plots indicated that relationships were not linear. Therefore, Spearman rank correlation coefficients were calculated, and locally weighted regression (LOESS)^(15,16) was used to explore the unusual patterns in the data without specifying a parametric form of the regression model. The fitting was carried out using the LOESS procedure in SAS (SAS Institute, Inc., Cary, N.C.). The order of the polynomial was 1. The smoothing parameters were chosen by finding the smoothing parameter with the minimum global AICC (bias corrected Akaike information criterion).⁽¹⁷⁾ In cases where the criterion failed to pick up a smooth curve, a smoothing parameter was chosen to be a value as large as possible while the fitted curve represented the pattern in the data smoothly.

The average estimated high cumulative asbestos exposure in this study population was 3.6 times the average low cumulative asbestos exposure, and the corresponding estimated welding fume cumulative average ratio was 6.7. This suggests a substantial range of estimated cumulative exposure to the confounders in this study population that potentially could influence the risk estimates for ionizing radiation and lung cancer.

The changes in relative risk for asbestos and welding fume, on the other hand, were not of primary interest, since those risks are already known. Therefore, an analysis was carried out to assess the effect of the range of exposure estimates to asbestos and welding fume on the risk estimates for radiation and lung cancer. Each worker's cumulative exposures to asbestos and welding fume were recalculated using his or her own work history and the low and high intensity estimates for each cell of the asbestos and welding fume exposure matrices.

As in the original analysis, which used the final intensity estimates,⁽⁶⁾ conditional logistic regression using PECAN in Epicure (v. 2.10; Hirosoft International Corporation, Seattle, Wash.) was carried out two more times, first using the lowest and then the highest calculated cumulative exposure for each worker for both asbestos and welding fume. This multivariate analysis was designed to evaluate the robustness of the external ionizing radiation-lung cancer risk estimates, while adjusting for potential confounders such as gender, radiation monitoring status, smoking habit surrogates (SES and birth cohort), welding fumes, and asbestos. In the analysis, all variables except asbestos and welding fume cumulative exposures were held constant. The main regression model was log-linear. Odds ratios (ORs) and the corresponding 95% profile likelihood-based confidence intervals (CIs) were derived from parameter estimates and the associated standard errors of the regression model.

TABLE I. Final Cumulative Exposure Estimates, Stratified into Exposed-Only Workers and All Workers

Exposure Hazard	N	Min	Max	Median	Mean	TLV	% > TLV-1	% > TLV-10	Percent Exceedance	
									Cumulative TLV ^A	
Exposed Workers Only ^B										
Asbestos (f-d/cm ³)	2796	0.01	19800	29	790	0.1 f/cm ³	59	27	32	
Welding fume (mg-d/m ³)	2318	0.16	30200	600	1800	5 mg/m ³	31	3.8	1.4	
Chromium (μg-d/m ³)	266	0.23	3940	400	740	10 μg/m ³	7.5	0.0	0.0	
							REL ^C	% REL-1	% REL-10	Percent Exceedance Cumulative REL ^A
Nickel (μg-d/m ³)	371	0.42	7630	980	1600	15 μg/m ³	14	0.0	0.0	
All Workers in Study Population										
Exposure Hazard	N ^D	Min	Max	Median	Mean	TLV	% > TLV-1	% > TLV-10	Percent Exceedance Cumulative TLV	
Asbestos (f-d/cm ³)	4386	0.01	19800	22	520	0.1 f/cm ³	46	18	20	
Welding fume (mg-d/m ³)	4386	0.03	30200	160	1000	5 mg/m ³	16	2.0	0.8	
Chromium (μg-d/m ³)	4386	0.00	3940	^E	^E	10 μg/m ³	0.5	0.0	0.0	
							REL	% > REL-1	% > REL-10	Percent Exceedance Cumulative REL
Nickel (μg-d/m ³)	4386	0.00	7630	^E	^E	15 μg/m ³	1.1	0.0	0.0	

^APercent of workers whose cumulative exposure exceeded their respective cumulative ACGIH threshold limit value (TLV) or REL.

^BWorkers who had at least one work history segment with an exposure to the hazard above background.

^CThe NIOSH recommended exposure limit (REL, 15 μg/m³) is used for nickel due to its considerably lower value compared with the TLV.

^DTwo workers had no exposure assigned to them due to an incomplete work history, hence N = 4386.

^EValues not calculated due to heavily censored data distribution.

RESULTS

Estimates of Individual Workers' Cumulative Exposures

In Table I, summary statistics for the four contaminants are stratified into all workers (the entire lung cancer case-control population), and workers within the population who were ever exposed (at least one job in the employment history was exposed above background intensity). Exposed workers' lifetime cumulative exposure estimates to asbestos ranged from 0.01 fiber-days/cm³ to just under 20,000 fiber-days/cm³, with a median of 29 fiber-days/cm³ and an arithmetic mean of 790 fiber-days/cm³.

For the entire population, the numbers are similar except that the median and mean exposures, and the percentages greater than comparison TLVs, are lower, as would be expected. Note that it is possible for the minimum cumulative values for asbestos exposure to be the same (within rounding error) for all workers and "exposed only" workers due to the way intensities were assigned, and the way that cumulative exposures are calculated. "Unexposed" workers in this population were defined as those who had only a background exposure (nonzero exposure) in their work history.

Because the exposure was nonzero, if a worker had a very long work history, his cumulative exposure could be the same or even exceed that of another worker who had a "Very Low" intensity of exposure, and who worked for a very short time period (as little as 1 day).

Approximately 32% of asbestos-exposed workers at the site were exposed in excess of the cumulative TLV based on his/her own duration of exposure, 59% of asbestos-exposed workers at the site were exposed to cumulative exposures in excess of the TLV-1 (24 fiber-days/cm³), and approximately 27% in excess of the TLV-10 (240 fiber-days/cm³, Table I). Among all workers in the case-control population, 20% of workers were exposed in excess of their cumulative TLV, 46% were exposed in excess of the TLV-1, and 18% in excess of the TLV-10.

Similarly, exposed workers' estimated cumulative exposures to welding fume ranged from 0.16 mg-days/m³ to just over 30,000 mg-days/m³, with a median of 600 mg-days/m³ and an arithmetic mean of 1800 mg-days/m³. Only 1.4% of welding fume-exposed workers were exposed in excess of the cumulative TLV, but 31% of welding fume-exposed workers had cumulative exposures in excess of the TLV-1, and 3.8% in excess of the TLV-10 (Table I). Among all case-control population workers, 0.8%, 16%, and 2% had cumulative

exposures in excess of the cumulative TLV, TLV-1 and TLV-10, respectively.

Among chromium-exposed workers, none (0%) exceeded the calculated cumulative TLV, 7.5% had cumulative exposures greater than the equivalent TLV-1 level, and none (0%) had cumulative exposures greater than the TLV-10 equivalent level. With respect to cumulative nickel exposure estimates, none (0%), 14%, and 0% of nickel-exposed workers were exposed at a level greater than equivalents to their cumulative REL, the REL-1 and REL-10, respectively. Even smaller proportions of all case-control study workers had cumulative chromium or nickel estimated exposures greater than the levels equivalent to the TLV-1 (chromium) or REL-1 (nickel). Fewer workers were exposed to chromium or nickel in welding fume, as compared with welding fume, and these workers had lower exposures relative to the relevant cumulative guidelines.

Estimates and Trends over Time

Figure 1 illustrates the trend in geometric mean annual cumulative exposure estimates to asbestos in standardized job titles over the time period of the study, and Figure 2 shows the trends in annual cumulative exposure estimates for four highly exposed job titles. Figures 3 and 4 are comparable figures detailing the trends in welding fume exposures. Similar figures are not presented for chromium and nickel due to the small

number of jobs estimated to be exposed, and the instability of the resulting means.

As shown in Figure 1, among the “highly exposed” job titles (originally estimated by the panel to be in the medium or high exposed categories), the geometric mean of the cumulative annual exposure estimates for asbestos dropped from about 270 fiber-days/cm³/year in 1972, to 21 fiber-days/cm³/year in the 1978–1980 time-period, and to less than 2 fiber-days/cm³/year in the 1981–1983 time period and thereafter. Based on qualitative information from records at the shipyard, verified by the panel members, this was due to more stringent monitoring and the introduction of better engineering controls, work practices, and respiratory protection about that time.

Respiratory protection, which became required for asbestos work during and after 1977, accounted for the largest portion of this decrease. In addition, after 1981, exposures were more tightly controlled and limited to certain job titles (mainly insulators and pipefitters and some power plant jobs). The percentage of exposed job titles within the study population dropped from 25% in 1945 to 5.5% in 1993 (Figure 1).

Figure 2 shows how panel-estimated exposures for a few highly exposed job titles varied over the study time period. Superimposed on this figure are some notes about significant changes in procedures that could have affected exposures, which are based partly on timelines compiled from hardcopy shipyard records and reports and partly on comments obtained

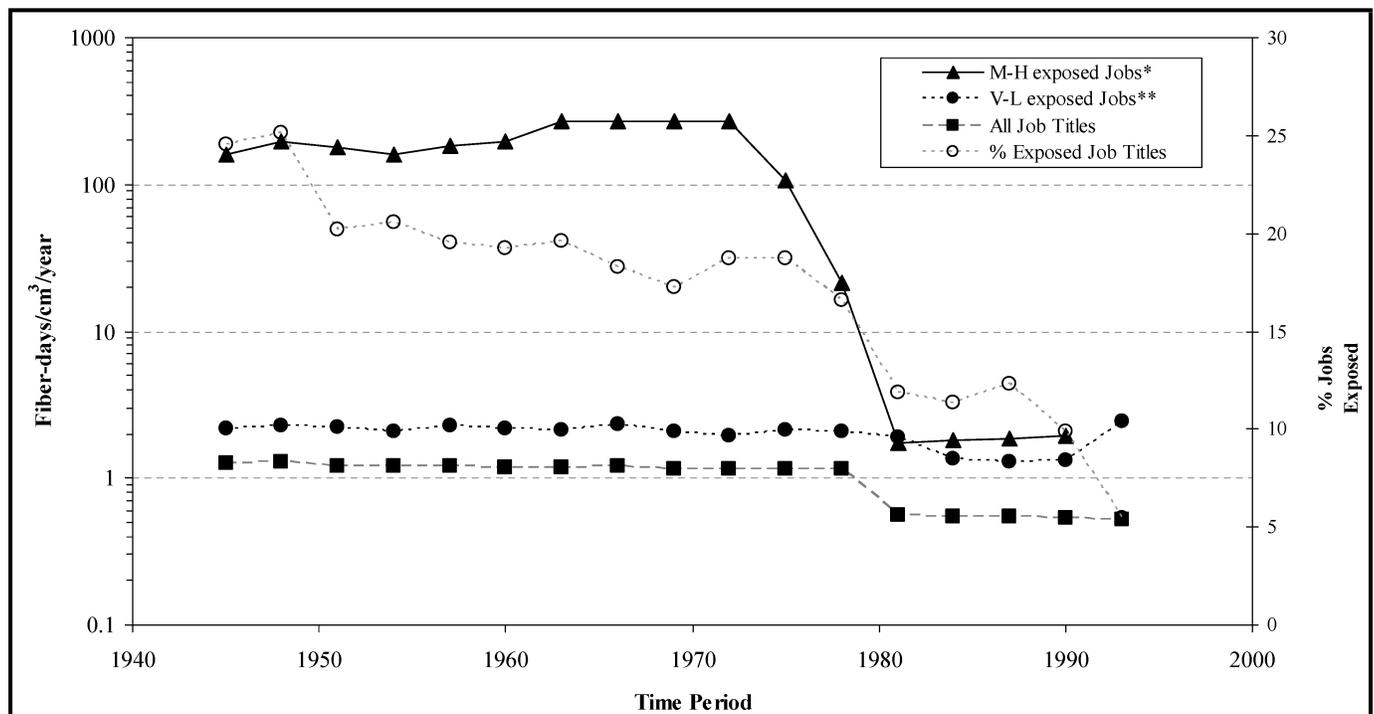


FIGURE 1. Geometric mean of annual asbestos exposure estimates from 1945 to 1995 by 3-year time periods for qualifying job titles. *Original estimated intensity was medium (M) or high (H); ** very low (V) or low (L); All Job Titles includes unexposed jobs, to which a nonzero background intensity was assumed. There were 1174 standardized job titles in the data set.

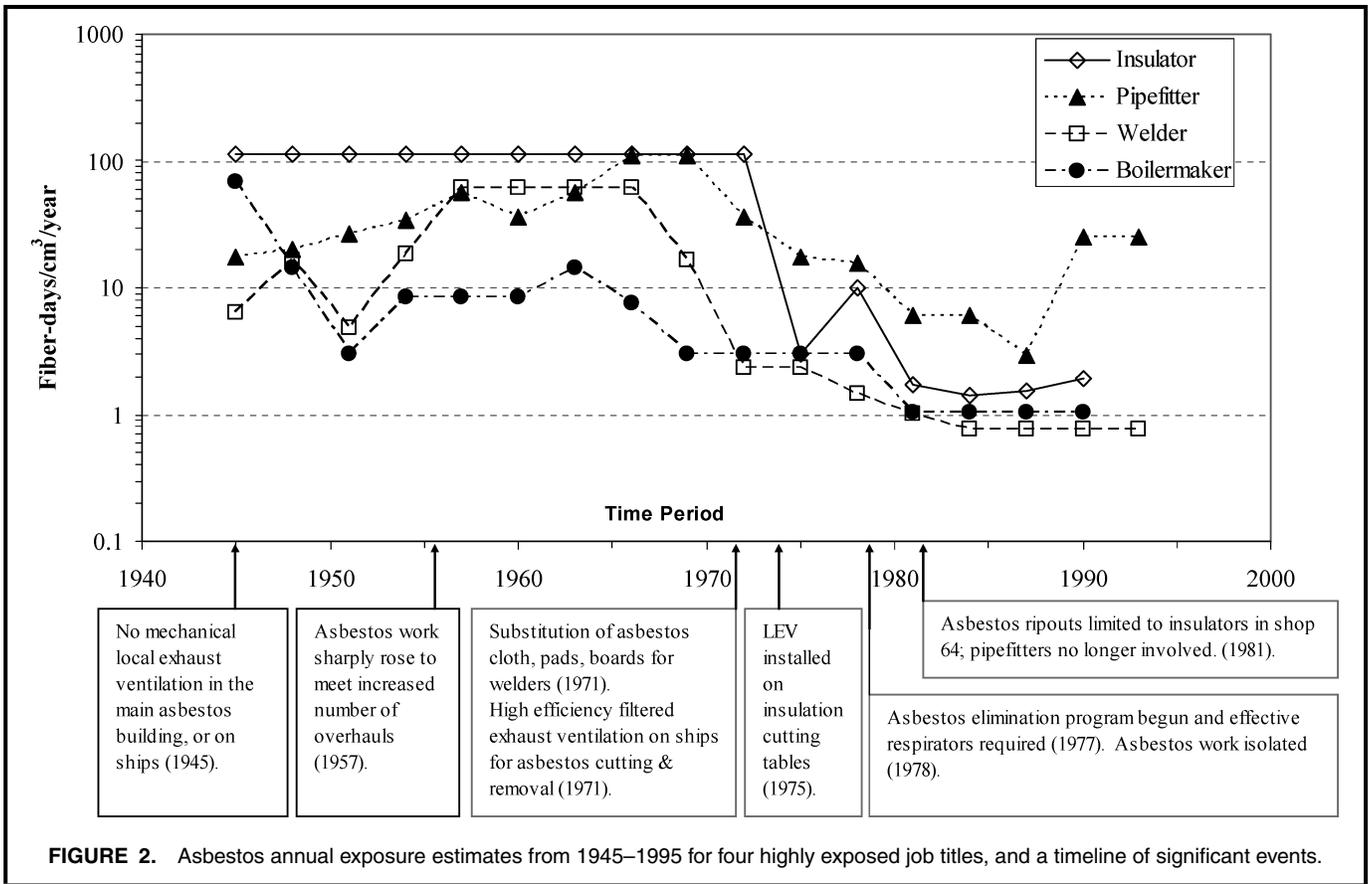


FIGURE 2. Asbestos annual exposure estimates from 1945–1995 for four highly exposed job titles, and a timeline of significant events.

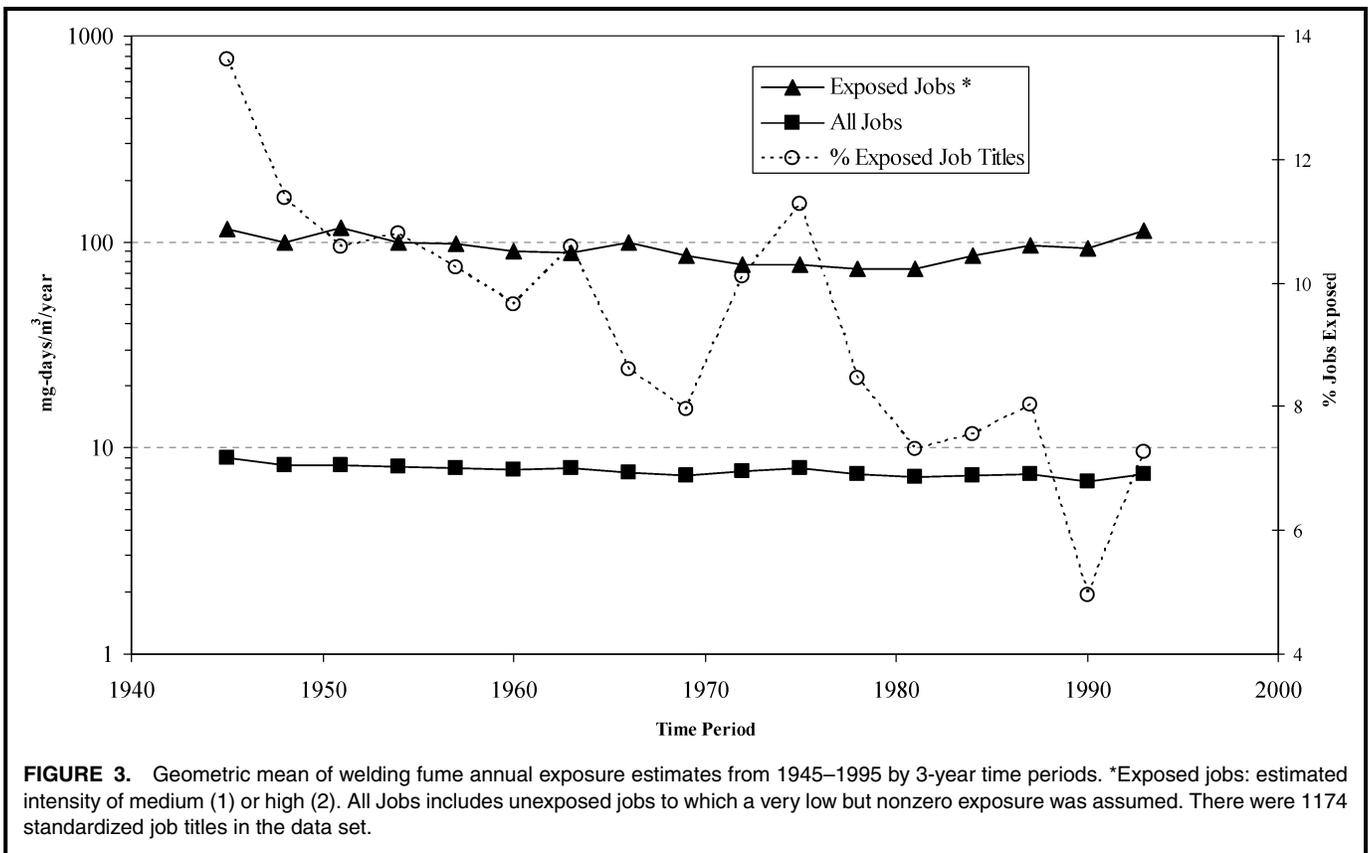


FIGURE 3. Geometric mean of welding fume annual exposure estimates from 1945–1995 by 3-year time periods. *Exposed jobs: estimated intensity of medium (1) or high (2). All Jobs includes unexposed jobs to which a very low but nonzero exposure was assumed. There were 1174 standardized job titles in the data set.

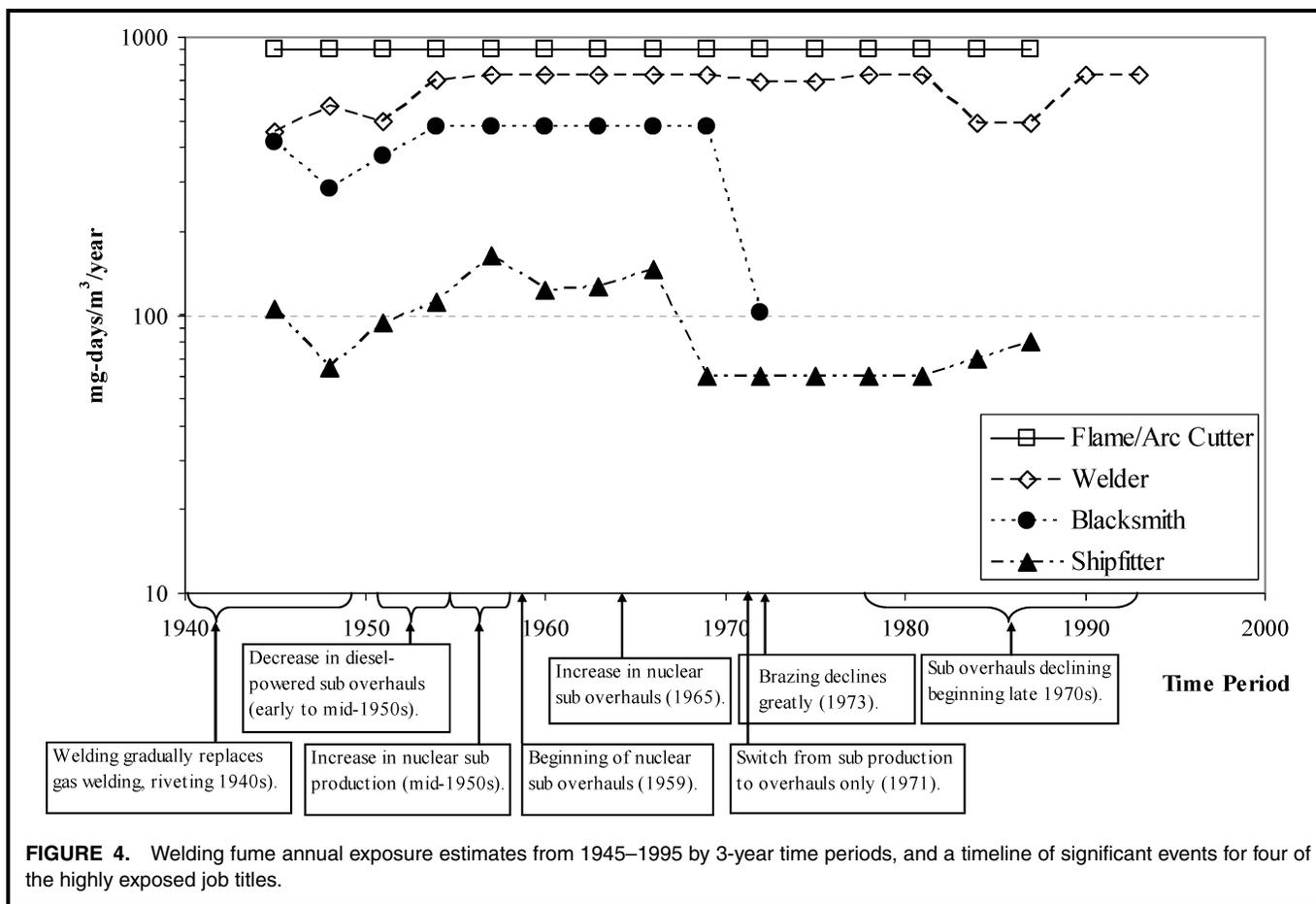


FIGURE 4. Welding fume annual exposure estimates from 1945–1995 by 3-year time periods, and a timeline of significant events for four of the highly exposed job titles.

from panel members during the estimation process and during the follow-up consensus meetings.

For example, pipefitter exposures (Figure 2) after 1981 dropped because pipefitters were no longer performing major insulating tasks. Insulating jobs (ripouts) were transferred to the woodworking shop from the pipe shop. Pipefitters' exposures appeared to rise from the early years to about 1970. This may have been due to a sharp increase in asbestos work due to an increased number of ship overhauls starting in the mid-1950s. After 1971, welders' exposures were likely reduced by substitution of asbestos cloth, pads, and boards for welders in 1971. In addition, increased use of high-efficiency filtered local exhaust ventilation during asbestos work on ships occurred about the same time.

A variable pattern of annual exposure estimates to welding fume was evident over the years (Figures 3 and 4). Figure 3 shows no obvious trends in geometric mean exposures among exposed jobs. Geometric means in 1945 were 120 mg-days/m³/year, 73 mg-days/m³/year in the 1978–1980 time-period, and 110 mg-days/m³/year in the 1993–1995 time-period. Because respiratory protection was not required in the later years in most welding operations as they were in asbestos operations, that factor would not have had a similar effect. Improvements in local exhaust ventilation used on ships and in welding shops may have resulted in the apparent slight dip in mean exposures in the middle of the time period.

In addition, there was a sizable reduction in brazing beginning in 1973, resulting in a compensating increase in ferrous welding. Thus, even as the number of ship overhauls declined after the mid-to-late 1970s, exposures remained high. The percentage of exposed jobs dropped from about 14% in 1945 to about 7% in 1993, reflecting the fact that fewer workers were exposed over time, but that the frequency and intensity of exposure may have increased to those workers exposed.

As shown in Figure 4, there is little or no apparent trend in the flame/arc cutter or welder job titles. Among shipfitters, there is a dip in annual cumulative exposure estimates beginning in the 1969–1971 time-period. This is largely due to the drop in frequency of welding in the shipfitter job category, as estimated by the expert panel. Estimated frequencies of welding exposures in shipfitters dropped from typically 90 days (38% of working days) prior to this time period to about 20 days (8% of working days) thereafter. This drop may be linked to the switch from a mix of new construction and overhauls to overhauls only (no new construction) in 1971.

Correlations of Exposure Agents

An important question that arose during the study was whether exposures of study population members to asbestos, welding fume, and ionizing radiation were substantially correlated, such that the effects of these exposures on rates of lung cancer could not be easily separated. To examine this

TABLE II. Spearman Rank Correlation Coefficients Between Estimates of Cumulative Exposure to Total Radiation, Occupational Radiation, Asbestos, and Welding Fume

Exposure Agent, Lag	Cumulative Total Radiation Exposure ^A	Cumulative Occupational Radiation Exposure ^B	Asbestos (All Workers)	Asbestos (Exposed Only) ^C
All workers	Coefficient ^D (N) ^E	Coefficient ^D (N) ^E	Coefficient ^D (N) ^E	Coefficient ^D (N)
Asbestos, no lag	0.43 (4024)	0.13 (1563)	—	
Asbestos, 15-year lag	0.41 (3354)	0.14 (1163)	—	
Asbestos, 20-year lag	0.41 (2929)	0.11 (927)	—	
Asbestos, 25-year lag	0.37 (2322)	0.09 (614)	—	
Welding fume, no lag	0.44 (4024)	0.19 (1563)	0.68 (4386)	
Welding fume, 15-year lag	0.42 (3354)	0.18 (1163)	0.70 (4005)	
Welding fume, 20-year lag	0.39 (2929)	0.15 (927)	0.72 (3688)	
Welding fume, 25-year lag	0.37 (2322)	0.14 (614)	0.73 (3249)	
Welding fume, no lag (Exposed only) ^C				0.30 (2045)

^AFrom all sources, including diagnostic medical X-rays.

^BExcluding diagnostic medical X-rays.

^CWorkers exposed above background to both asbestos and welding fume, no lag.

^DAll correlation coefficients were statistically significant ($p < 0.05$).

^ESample sizes vary because not all workers in the population had occupational or medical X-ray exposure, and because lags reduced sample sizes. In all cases, the equivalent lags were applied to both variables being correlated (e.g., radiation, welding fume, and asbestos).

possibility, scatter plots of the individual workers' cumulative exposures to asbestos, welding fume, and ionizing radiation were examined, and Spearman rank correlation coefficients were calculated (Table II).

The Spearman rank correlation coefficients between asbestos and welding fumes (Table II) ranged from 0.68 to 0.73 for all workers depending on the amount of lag, indicating a moderately strong relationship between the variables. All of the correlations in Table II were statistically significant ($p < 0.05$), again due in large part to the very large sample size.

When the analysis is limited to workers exposed exclusively above background levels to both asbestos and welding fume, the Spearman rank correlation coefficient (Table II) drops to 0.30 ($N = 2045$), compared to 0.68 overall.

The most important question was whether there was a statistical association between radiation dose and cumulative exposures to asbestos or welding fume in this population. Associations were examined separately using total radiation dose (including medical dose, such as from chest X-rays) and occupational radiation dose (excluding medical dose). Spearman correlation coefficients (Table II) between cumulative asbestos exposures and total cumulative radiation doses ranged from 0.37 to 0.43, and those between asbestos and cumulative occupational dose ranged from 0.09 to 0.14.

The correlations between welding fume and radiation dose show a very similar picture. From Table II, it appears that the correlations with occupational radiation dose are quite weak, while the correlations between both asbestos and welding fume and total radiation dose are weak to moderate.

Photofluorographic chest examinations resulted in 82% of the dose from medical sources, and radiation workers received

26% of their collective dose from WRX.⁽¹⁸⁾ The cumulative effect of the annual X-ray doses would result in many workers having the same or a very similar cumulative dose over their working lifetime, especially in those with relatively low occupational dose.

In addition, although correlations between asbestos, welding fume, and total radiation dose were slightly higher than those with occupational radiation dose, addition of work-related medical X-ray doses to the models attenuated the risk estimates and were nearly flat in multivariate analysis, as explained by Yiin et al.⁽⁶⁾ Because the inclusion of WRX diluted the differences in dose between cases and controls, this result is not unexpected. Addition of asbestos and welding to the model did not further reduce these attenuated estimates; i.e., removing these two variables had absolutely no impact on the total radiation dose RR or ERR.

High and Low Exposure Estimates and Effect on Risk of Lung Cancer

Table III is a brief summary of the risk results using the lowest and highest set of exposure estimates to asbestos and welding fume, as well as the final exposure estimates in the original analysis. Incorporating either lowest or highest estimates of exposure intensity to asbestos and welding fume (treated as confounders) has no effect on the lung cancer risk estimates with total or occupational ionizing radiation dose in this population. There also was only a very slight if any effect on the relative risk estimates for exposure to asbestos and welding fume and lung cancer in the multivariate analysis.

TABLE III. Multivariate Analysis—Conditional Logistic Regression of Lung Cancer Risk with Radiation Exposure (with a 15-year lag), and Potential Confounders at PNS; Comparison of Relative Risks Assuming Lowest, Final, and Highest Intensity Estimates for Asbestos and Welding Fume

	Risk Estimate (95% CI) Low Intensity Estimates	Risk Estimate (95% CI) Final Intensity Estimates	Risk Estimate (95% CI) High Intensity Estimates
Welding fume (at 1,000 mg-days/m ³)	RR = 1.01 (0.89, 1.13)	RR = 1.01 (0.98, 1.04)	RR = 1.00 (0.98, 1.03)
Asbestos (at 1000 f-days/cm ³)	RR = 1.10 (0.91, 1.32)	RR = 1.02 (0.98, 1.07)	RR = 1.03 (0.98, 1.08)
<i>Occupational radiation dose</i>			
Log-linear ^A (at 10 mSv)	RR = 1.02 (0.99, 1.04)	RR = 1.02 (0.99, 1.04)	RR = 1.02 (0.99, 1.04)
Linear ^A (per 10 mSv)	ERR = 1.9% (−0.9%, 6.6%)	ERR = 1.9% (−0.9%, 6.6%)	ERR = 1.8% (−0.9%, 6.5%)

^AModel with all potential confounders including sex, radiation monitoring status, socioeconomic status, and exposures listed above modeled log-linearly or linearly. RR and the corresponding 95% CI for these potential confounders (from the log-linear model) are very similar whether occupational dose is modeled log-linearly, linearly, or categorically.

DISCUSSION

The primary goal of the nested case-control study of lung cancer at the Portsmouth Naval Shipyard was to help clarify whether any relationship existed between protracted, low-dose exposure to external ionizing radiation and lung cancer.⁽⁶⁾ To do this more effectively, it was important to estimate some of the other worker exposures at the shipyard and, if possible, determine the degree to which these concomitant exposures were associated with radiation doses received by the workers or were associated with each other. Confounding (as well as misclassification of exposures) is an issue that is frequently listed as a limitation in epidemiologic studies.⁽¹⁹⁾

However, unless the associations of the confounding agents with both the postulated health effect and the agent of interest are strong, the impact is not likely to be large.⁽²⁰⁾ It is known that both asbestos⁽²¹⁾ and welding fumes⁽⁷⁾ have the potential to induce lung cancer. Thus, it is important to examine the level of exposure to these agents, the proportion of the population exposed to the confounding agents, and any potential associations of external ionizing radiation dose (within members of the study population) with asbestos and welding fume.

The frequency distributions for estimated exposures to asbestos and welding fume indicate that a fairly large proportion of the workforce was exposed at the shipyard over time. This is consistent with observations at the shipyard and from industrial hygiene documentation available from the site. Among the 4388 workers in the case-control study population, 2796 workers (nearly 64%) were ever exposed to asbestos, and 2318 (53%) were ever exposed to welding fume.

On the other hand, fewer workers were exposed to nickel and chromium from welding processes. This is consistent with the observation that the great majority of welding was mild-steel welding, for which the primary exposure was iron oxide fume. This was true even after the introduction of nuclear engines, and associated use of stainless steel, in the late 1950s.

Only about 266 workers in the case-control study population were exposed to chromium in welding fume, and 371 to nickel in welding fume.

Among all workers in the study population, cumulative exposures to asbestos appeared to be moderately to strongly associated with welding fume cumulative exposures, but among those exposed, only above background intensities the correlation was far weaker. When workers exposed only to background levels of asbestos and welding fume were excluded, the correlation in cumulative exposures between these two contaminants dropped substantially from about 0.68 to 0.30. Clearly, the higher correlations over the entire study population were influenced by the perfectly correlated durations and identical exposures among the very large proportion of workers in the population exposed only to background levels (N = 2070 or about 47% of the population).

Cumulative estimated asbestos and welding fume exposures were only very weakly associated with occupational radiation dose and only weakly to moderately associated with total radiation dose. The slightly stronger correlations with total radiation dose are likely due, in part, to most asbestos workers being enrolled in an asbestos-exposed worker surveillance program at PNS, which required more frequent chest X-rays, particularly after 1980.

In addition, asbestos and welding fume cumulative exposures were, in part, driven by duration of employment or duration of exposure, as were cumulative doses to ionizing radiation. The quite weak associations between welding fume or asbestos exposures and occupational radiation exposures are due to the way the work was organized at the shipyard. Radiation exposures on board nuclear-powered ships were generally confined to the shielded reactor compartments, and the refueling operation was done by removing and quickly replacing the reactor core. In addition, refits and repairs were usually more frequent than refueling operations. Incorporation of WRX in the analyses attenuated the risk estimates.⁽⁶⁾ This was attributed to the dilution of exposure differences between cases and controls.

CONCLUSIONS

The estimated exposures presented here suggest that a fairly large proportion of workers in this population were exposed to asbestos and welding fume, but that exposures to chromium and nickel were lower and affected fewer workers. There was little or no obvious trend in exposure to welding fume from 1945 to 1996, but a large decrease in asbestos exposure occurred after the mid-1970s due mainly to the tightening of requirements for respiratory protection and exhaust ventilation in asbestos work.

Weak relationships were seen between monitored lifetime cumulative occupational radiation dose and estimated asbestos or welding fume cumulative exposures. The inclusion of work-related X-ray dose in multivariate models resulted in attenuation of the lung cancer risk ratios, and the inclusion of exposures to the potential confounders and asbestos and welding fumes in the risk models had no effect on the risk estimates for either total or occupational radiation. It is thus unlikely that the degree of co-linearity seen in this population confounded the lung cancer-radiation risk estimates.

A moderately strong relationship was seen between asbestos and welding fume for all workers in the study, but the correlation was very weak when including only ever-exposed workers to both agents. The moderately strong relationship seen among all study-population workers was heavily influenced by a high correlation between the preponderance of unexposed workers.

Analyses carried out to assess the robustness of the health risks with different values of asbestos and welding fume estimates (when treated as confounders) indicated that the range of exposures to asbestos and welding fume estimated for subjects in this study had no effect on relative risk or excess relative risk of lung cancer related to external ionizing radiation dose.

The detailed exposure assessment conducted at the PNS provided estimates useful not only for reconstruction of historical exposures at the shipyard but also allowed an assessment of the co-linearity of the most important exposures to PNS study workers. This assessment in turn allowed a more detailed analysis of dose and response to these agents than would otherwise have been possible.

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