CME Available for this Article at ACOEM.org

# Retrospective Cohort Mortality Study and Nested Case–Control Study of Workers Exposed to Creosote at 11 Wood-Treating Plants in the United States

**Otto Wong, ScD**
**Fran Harris, MS**

## Learning Objectives

- Summarize data on overall mortality, deaths from site-specific cancers, and deaaths from non-malignant disorders taken from a retrospective study of more than 2,000 employees potentially exposed to creosote in the form of either wood preservatives or wood products treated with creosote-containing products.
- Describe the relationship, if any, between cancer deaths and years of employment for hourly workers, who were at higher risk of exposure to creosote than were salaried employees.
- Recall the mortality risk associated with lung cancer and multiple myeloma in a nested case-control study employing multivariate logistic regression analyses.

## Abstract

***Objective:*** *The objective of this study was to assess both malignant and nonmalignant mortality risks of workers exposed to creosote. For background, a literature review is also presented.* ***Materials and Methods:*** *The retrospective cohort study consisted of 2179 employees at 11 plants in the United States where wood (primarily railroad ties and utility poles) is treated with creosote-based preservatives. The observation period covered 1979–2001. Mortality data in the cohort study were analyzed in terms of cause-specific standardized mortality ratios (SMRs) and 95% confidence intervals (95% CIs), with expected deaths based on U.S. national cause-, gender-, race-, year-, age-specific mortality rates. In addition to the cohort investigation, a nested case–control study of lung cancer and multiple myeloma was conducted. Information on tobacco consumption and detailed employment (job titles) was obtained for cases and matched controls. Jobs were classified into 5 categories according to potential for exposure to creosote. Odds ratios (ORs) and 95% CIs were calculated for job categories and length of exposure.* ***Results:*** *Overall mortality for the entire cohort was lower than expected (293 observed deaths vs. 325.37 expected, SMR = 90.1, 95% CI = 80.0–101.0). Close to 90% employees were hourly, whose potential for exposure was generally much higher than that of salaried employees. Among hourly employees, except for multiple myeloma, none of the specific cancer sites showed any significant increase. Furthermore, detailed analysis by length of employment did not reveal any significant mortality excess or upward trend. Six deaths were from multiple myeloma, whereas 1.50 deaths were expected (SMR = 401.1, 95% CI = 147.2–873.1). However, analysis by length of employment did not show any upward trend for multiple myeloma. No significant mortality increase was reported for any nonmalignant disease, and analysis by length of employment did not reveal any upward trend. In the case–control study, an increased risk of lung cancer was associated with tobacco consumption (OR = 4.92) but not with any job/exposure category. For example, the lung cancer odds ratio for routine exposure to creosote-based wood preservatives was 0.58 (95% CI = 0.11–3.03). Similarly, case–control analyses of multiple myeloma did not reveal any association with employment at the plants or with exposure to creosote-based wood preservatives or to creosote-treated products.* ***Conclusion:*** *Based on the present investigation and other studies, there was no evidence that employment at the 11 wood-treating plants or exposure to creosote-based wood preservatives was associated with any significant mortality increase from site-specific cancers or nonmalignant diseases. Some results should be interpreted with caution because they were based on small numbers.* (J Occup Environ Med. *2005;47:683–697*)

From Applied Health Sciences, Inc., San Mateo, California (Dr Wong, Ms. Harris); the Department of Epidemiology, Tulane University, New Orleans, Louisiana (Dr Wong); the Department of Community Medicine, Chinese University of Hong Kong, Hong Kong (Dr Wong); Department of Community Medicine, University of Hong Kong, Hong Kong (Dr. Wong); the School of Public Health, Fudan University, Shanghai, China (Dr Wong); and the School of Medicine, University of California, San Francisco, California (Ms. Harris).

Otto Wong has no commercial interest related to this article.

Address correspondence to: Otto Wong, ScD, Applied Health Sciences, Inc., 181 Second Avenue, Suite 628, San Mateo, CA 94401. E-mail: ottowong@aol.com.



**DOI: 10.1097/01.jom.0000165016.71465.7a**

Creosote is a mixture of more than 150 compounds derived from the distillation of coal tar and is used primarily in wood preservatives to kill both fungi and boring insects such as shipworms and termites that are likely to infest wood. Creosote is a heavy, oily liquid with a sharp and smoky smell. It is irritating to the skin and its vapors can produce a burning sensation to the eyes and the upper respiratory system.

In the United States, more than 500 kg/m$^2$ of creosote are produced annually. Creosote-based wood preservatives are used to treat wood products such as railroad ties, utility poles, and building lumber. The conventional wood-treating process consists of impregnating wood products with creosote-based preservatives in enclosed pressurized cylinders or "retorts." The cylinders are equipped with manual or hydraulic doors, and wood products are moved in and out of the cylinders on trams. The development of mechanical and material-handling equipment over the years has resulted in the gradual reduction of direct contact by wood-treating workers with the preservatives or treated wood products.

The long-term health effects of occupational exposure to creosote-based wood preservatives have been investigated in several epidemiologic studies. Most of the studies were conducted in Sweden. Flodin et al[1] conducted a hospital-based case–control study of multiple myeloma in

central and southeastern Sweden. The study consisted of 131 patients diagnosed with multiple myeloma between 1973 and 1983, who, as noted by the investigators, represented approximately one third of the cases that occurred in the same areas as identified by the regional cancer registry. As the basis for comparison, Flodin et al[1] used 431 community controls, with approximately half of them originally selected for a case–control study of chronic lymphocytic leukemia.[2] The average ages of the cases and the controls were 64 and 58 years, respectively. Employment information was obtained from a mail questionnaire. Seven cases and four controls were reported to have been exposed to creosote. The risk ratio (RR) of multiple myeloma in relation to exposure to creosote was 4.7 and the 95% confidence interval (95% CI) was 1.2–18.0.

As noted by the authors, the Flodin et al[1] study had a number of limitations. First, the ascertainment of cases was incomplete, which might have distorted the distribution of occupations among the cases. Second, the cases were older than the controls (average ages of 64 vs. 58 years), and "age over 60" was found to be a significant risk factor in the study (RR = 3.0, 95% CI = 2.0–4.6). Third, the response rate was higher among the cases (96%) than among the controls (80%), which might be indicative of potential reporting bias. Fourth, the "time window" for exposure in the study was inconsistent between the cases and the controls. Therefore, the exposure information might not be comparable between the cases and the controls. Finally, the definition of "exposure to creosote" appeared to be overly broad. For example, electrical linemen were considered to be exposed, although the only source of exposure for electrical linemen would be utility poles previously (regardless of how long ago) treated with preservatives (not necessarily creosote-based). In any event, as cautioned by Flodin et al,[1] the number of exposed individuals was small, which made the reported association less convincing.

Persson et al[3] reported the results of a hospital-based case–control study of malignant lymphomas (Hodgkin disease and non-Hodgkin lymphoma, [NHL]) from Sweden. The 106 cases were diagnosed with NHL between 1964 and 1986. The 275 controls were selected among those originally chosen for two previous studies of multiple myeloma and chronic lymphocytic leukemia.[1,2] Information on employment was obtained from the same questionnaire that was used in the Flodin et al[1,2] investigations. Five NHL cases and one control were reported to have been exposed to creosote. The NHL RR for creosote was 9.4 (90% CI = 1.2–69).

The Persson et al[3] study of NHL used the same methodological approach and the same questionnaire and shared some of the same controls as in the previous Flodin et al[1,2] studies of multiple myeloma and chronic lymphocytic leukemia. Therefore, many comments on the Flodin et al[1] study would be applicable to the Persson et al[3] study as well. Among the controls selected in the Persson et al[3] study, only one was exposed to creosote. Persson et al[3] remarked: "There remains apparently the possibility that exposure to creosote for some reason has been underestimated among the referents in common." In the paper, Persson et al[3] reported 90% confidence intervals. Based on the information provided in the paper, the 95% CI of the RR for creosote would have been 0.82–108, not statistically significant at the 5% level. The extremely wide confidence interval should also be noted, which is indicative of the small underlying number (only one exposed control).

The results of a cohort study of 922 creosote-exposed impregnators employed at 13 plants in Sweden and Norway for at least 1 year between 1950 and 1975 were reported by Karlehagen et al.[4] Cancer cases among cohort members were identified through the national cancer registries in the two countries. The follow-up periods were 1958–1985 in Sweden and 1953–1987 in Norway. Cancer risk was expressed in terms of standardized incidence ratios (SIR). The risk of nonmelanoma skin cancer was significantly elevated (SIR = 2.3, 95% CI = 1.08–4.50). Furthermore, there was a nonsignificant increase of melanoma skin cancer (SIR = 1.72, 95% CI = 0.56–4.01). The authors attributed the elevated skin cancer risk to a combination of exposures to creosote and sunlight. Except for nonmelanoma skin cancer, no other cancer was found to be significantly elevated. For example, the SIR for lung cancer was 0.79 (95% CI = 0.42–1.35) based on 13 cases. There were six cases of NHL, with an SIR of 1.89 (95% CI = 0.69–4.12).

Two aspects of the Karlehagen et al[4] study need further discussion. First, the data in the study partially overlapped those of the case–control studies by Flodin et al[1,2] and Persson et al.[3] Therefore, the results cannot be regarded as independent. Second, the increase of nonmelanoma skin cancer was restricted to the Swedish workers only. Throughout the study period, wood preservatives other than creosote were used at the Swedish plants, including mixtures of salts of copper, chromium, and arsenic. Karlehager et al[4] also pointed out that the impregnators worked outdoors and were exposed to sunlight. As such, the interpretation of the results of the study is complicated by potential concomitant exposures.

Eriksson and Karlsson[5] reported a population-based case–control study of multiple myeloma in Sweden. The cases were 275 patients diagnosed with multiple myeloma in four northern counties between 1982 and 1986. For each case, a matched control was selected. The study thus consisted of 275 cases and 275 matched controls. Information on occupation and exposure was obtained through the use of a questionnaire. Four cases and five controls were reported to have been

exposed to creosote. The RR for creosote exposure was 0.75 (90% CI = 0.21–2.51). Thus, the authors concluded that there was no increased risk of multiple myeloma in relation to creosote exposure.

Unlike the Persson et al[3] or the Flodin et al[1,2] studies, in the Eriksson and Karlsson[5] investigation, to minimize potential confounding, controls were matched individually to cases in terms of age, sex, county of residence, and vital status. However, similar to other population-based case–control studies, the exposure information in the Eriksson and Karlsson[3] study was based on questionnaires (ie, recalls) and was subject to potential bias and inaccuracy.

From the United States, Blair et al[6] reported the results of a population-based case–control study of NHL. The study consisted of 622 patients diagnosed with NHL in Iowa between 1981 and 1983 and in Minnesota between 1980 and 1982. A total of 1245 community controls were randomly selected and frequency-matched by state, age (within 5-year categories), and by year of death for deceased cases. Information on occupation and exposure was obtained from a questionnaire interview. Based on the judgment of one of the investigators, jobs were classified into "low" and "high" intensity of exposure. Fifty-three cases and 105 controls were reported to have been exposed to "asphalt and creosote," and the corresponding RR was 1.0 (95% CI = 0.7–1.5). The data were further analyzed in terms of intensity of exposure, and no upward trend was detected. The RRs were 1.0 (95% CI = 0.7–1.5) and 1.1 (95% CI = 0.3–4.6) for low- and high-exposure categories, respectively. The authors concluded: "In summary, this evaluation does not indicate that industrial exposures are a major contributor to the etiology of NHL."

One of the major strengths of the Blair et al[6] study was the large sample size. For example, the exposure category "asphalt and creosote" consisted of 53 cases and 105 controls. The stability of the findings was demonstrated by the relatively narrow confidence intervals. Unfortunately, the authors did not provide a separate analysis for creosote. In addition, the problems associated with information obtained from questionnaire (potential recall bias and inaccuracy) also apply to this population-based case–control study.

As indicated here, there are only a handful of epidemiologic studies in the literature that addressed the long-term health effects of chronic occupational exposure to creosote-based wood preservatives. Most investigators used the population-based case–control study design. Furthermore, most of the investigations were conducted in Sweden and the data in these studies overlapped. Thus, the Swedish studies were not independent. Furthermore, the literature review indicates that the results from these studies were not consistent. In addition, the interpretation of the findings from some of these investigations was complicated by various limitations such as incomplete case ascertainment, incomparability between cases and controls, potential reporting bias, overly broad exposure classification, and concomitant exposures to known carcinogens. Further research is needed to investigate the long-term health effects of workers exposed to creosote-based wood preservatives.

## Objective

The objective of the present investigation was to assess both malignant and nonmalignant mortality risks of workers employed at 11 industrial facilities in the United States that used creosote-based preservatives to treat wood products. This is the first cohort study of workers exposed to creosote in the United States that we are aware of.

## Materials and Methods

### Cohort Study

The retrospective cohort consisted of all individuals who were employed at 11 participating wood-treating plants in the United States between January 1, 1979, and December 31, 1999. The 11 plants are located in Green Spring (WV), Galesburg (IL), Grenada (MS), Guthrie (KY), North Little Rock (AK), Susquehanna (PA), Denver (CO), Feather River (CA), Florence (SC), Montgomery (AL), and Roanoke (VA). All 11 plants use the enclosed system of pressurized wood treating, and creosote-based wood preservatives are used at all 11 locations. The cohort members were identified through company employment records. Information abstracted from these records included social security number, name, gender, race, date of birth, date of employment, employment status on the closing date of the study, vital status on the closing date of the study, and date of retirement, separation, or death when applicable.

The vital status of cohort members as of December 31, 2001, was ascertained through several sources, including company personnel records, the Social Security Administration's Death Master File, and the National Center for Health Statistics' National Death Index (NDI). The Death Master File is a national database of all deaths reported to the Social Security Administration since 1939. Vital status of an individual is ascertained by matching the last name and social security number. The NDI, established in 1979, is a national death registry designed to facilitate health investigations. Matching is based on the full name, social security number, birth date, gender, race, and, in some cases, father's surname. Vital status information as well as causes of death of study subjects are provided by NDI through a service known as "NDI Plus." In the present study, causes of death for decedents were obtained from either NDI Plus

or death certificates. The underlying causes of death were coded or converted to the 8th Revision of the International Classification of Diseases (ICD).

Statistical analyses in the cohort study were based on cause-specific standardized mortality ratios (SMRs). Person-years of observation were classified by age (5-year groups), gender, race, and calendar year (5-year groups). Expected deaths were calculated by applying the U.S. national age-, cause-, gender-, race-, year-specific death rates to the corresponding person-years in the cohort. Cause-specific SMRs were computed by expressing the observed deaths as percentages of the expected. Also calculated were 95% confidence intervals (95% CIs). The actual calculations were performed through the University of Pittsburgh's OCMAP program.[7] Cause-specific mortality analyses were performed for the entire cohort, which included both hourly and salaried employees. Because most hourly workers were involved in a broad range of production and maintenance activities, their potential for exposure to wood preservatives or preservative-treated products was generally much higher that that of salaried employees. In addition to the overall analysis of the entire cohort, separate analyses were conducted for all hourly employees and for subcohorts of hourly employees stratified by length of employment and time since first employment (latency). Trend analyses by length of employment were based on the method described by Breslow and Day.[8] The significance of a trend is measured by the statistic chi-square with one degree of freedom.

In addition to analyses conducted using the routine OCMAP program, a special analysis for lymphohematopoietic malignancies was also performed. In the United States, because of the way in which mortality rates by ICD categories are tabulated by the National Center for Health Statistics (NCHS), analyses of non-Hodgkin lymphoma (NHL), multiple myeloma (MM), and specific leukemia cell types in most occupational cohort studies are generally not reported as such.[9–11] In the OCMAP program, NHL (ICD 200 and 202) appears in two categories: "lymphosarcoma and reticulosarcoma" (ICD 200) and "cancer of all other lymphatic and hematopoietic tissue" (ICD 202, 203, 208, and 209). Thus, part of NHL (ICD 202, "other lymphomas") is reported together with MM (ICD 203), polycythemia vera (ICD 208), and myelofibrosis (ICD 209). In the special analysis, NHL and MM were analyzed separately. In addition, a separate analysis for specific leukemia cell types was also performed. U.S. mortality rates for NHL, MM, and leukemia cell types compiled by the National Cancer Institute (NCI) based on data derived from the Surveillance, Epidemiology, and End Results (SEER) program were used in computing the expected deaths from these causes.[12–14]

## Nested Case–Control Study

In addition to the retrospective cohort study, a cohort-based or nested case–control study of lung cancer (ICD 162) and multiple myeloma (ICD 203) was conducted. Lung cancer was chosen because the SMR was slightly elevated for the entire cohort and information of smoking (a major confounder) was not available in the cohort study. Multiple myeloma was chosen because the SMR in the cohort study was significantly elevated. Workers in the overall cohort who died from lung cancer or multiple myeloma were the cases in the case–control study. Individually matched controls were selected at random from other decedents in the overall cohort who satisfied the following matching criteria: same plant, same gender, and similar age ($\pm$5 years) as the case. In addition, to ensure an equal opportunity for potential exposure, the control must have been alive at the time of death of the corresponding case. For each case, up to five controls (if available) were selected. For a few cases of lung cancer, no eligible control was found.

Additional information was collected for both cases and controls. Histories of tobacco use were obtained from coworkers. To avoid potential recall bias, lists of cases and controls were provided to these coworkers without revealing to the latter the case–control status of the study subjects. Detailed employment histories (consisting of specific job titles and dates) were abstracted from employment and other administrative records. For analysis, jobs of the cases and controls were classified into the following broad job/exposure categories.

*Routine exposure to creosote-based wood preservatives.* Jobs involving the handling of or contact with creosote-based wood preservatives on a routine basis such as oil unloaders, treating operators, treating supervisors, retortmen, retort crewmen, cylinder-changing operators, cylinder-changing crew, doormen (changing cylinders), test borers, and testing operators.

*Routine exposure to creosote-treated products.* Jobs involving the handling of creosote-treated products (railroad ties or utility poles) on a routine basis such as crane laborers, crane crewmen, dock loaders, and shipping supervisors.

*Intermittent exposure to wood preservatives and/or treated products.* Plantwide jobs involving assignments throughout the plant with intermittent exposure to wood preservatives and/or treated products such as maintenance crafts and general laborers who worked throughout the plant.

*Intermittent potential exposure to both treated and untreated materials.* Jobs involving the handling of both treated and untreated materials, resulting in potential intermittent exposure to treated products such as lift truck operators, prentice operators, locomotive operators, yard supervi-

sors, track crews, checkers, and heavy equipment operators.

*No or minimal exposure.* Jobs with no direct contact with wood preservatives or treated products such as log loader operators, boiler room firemen, mill crewmen, stock record clerks, office clerks, office managers, and truck drivers.

Some study subjects started working at the plants in the 1940s or 1950s, whereas comprehensive industrial hygiene monitoring at the plants began in the 1970s. Therefore, historical industrial hygiene data were not available for all the job categories for the exposure period covered by the retrospective cohort study. However, monitoring data were available for certain selected jobs for part of the exposure period. Because there was no specific regulatory standard for occupational exposure to creosote, concentration in terms of coal tar pitch volatiles − benzene soluble fraction (CTPV-BSF) was commonly used by regulators to determine exposure potentials to creosote. The Occupational Safety and Health Administration's (OSHA's) Permissible Exposure Level (PEL) for CTPV-BSF is 0.2 ($mg/m^3$). According to the available monitoring industrial hygiene data, 95% of the workers at the wood-treating plants were exposed to no more than 0.14 $mg/m^3$ CTPV-BSF.[15] In terms of specific jobs, the typical time-weighted average exposure of treating operators at the participating plants ranged from 0.04 to 0.11 $mg/m^3$ CTPV-BSF, with most measurements centered around 0.05 or 0.06 $mg/m^3$ CTPV-BSF. Because of the limited nature of monitoring data, the analyses will be based on job/exposure categories described here and not on specific industrial hygiene measurements.

Multivariate analyses based on conditional logistic regression were used in the case–control study to assess the relation between mortality from lung cancer or multiple myeloma and the following independent variables: tobacco consumption, length of employment, and job/exposure categories (using the category, "no or minimal exposure," as the reference). Matching was taken into consideration in the analyses. Odds ratios (ORs) or risk ratios (RRs) and 95% CIs were calculated. Chi-square with one degree of freedom was used for significance test. The multivariate analyses were performed using the SAS statistical programs.[16]

## Results

### Cohort Study

A total of 2179 employees at 11 wood-treating plants met the cohort definition and were eligible for inclusion in the retrospective cohort study. Selected demographic and employment characteristics of the cohort are provided in Table 1. The majority of the cohort members were male (92.2%) and hourly employees (87.2%). Half (50.3%) of the cohort members were hired before 1980, providing a potential latency period of 22 years or longer, which should be adequate for most chronic diseases. Approximately 60% of the cohort members were first employed before age 30. The average age at hire was 29.0 years. Approximately one third (34.6%) of the cohort members were employed for more than 15 years, and the average length of employment was 12.5 years. The maximum length of vital status follow up was 23 years (January 1, 1979, to December 31, 2001). The total number of person-years of observation was 36,317.

The number of observed and expected deaths, SMRs, and 95% CIs for selected causes for all cohort members are presented in Table 2. The total number of observed deaths (293) was fewer than the number of deaths expected (325.37). The corresponding SMR was 90.1 (95% CI = 80.0–101.0), close to being statistically significant. Mortality from all cancers was slightly higher than expected. The number of observed can-

**TABLE 1**
Descriptive Statistics of the Cohort of Workers at 11 Wood-Treating Plants

| Variable | | Number | Percentage |
|---|---|---|---|
| Total employees | | 2179 | 100.0 |
| Total person-yr | | 36,317 | 100.0 |
| Gender | Male | 2010 | 92.2 |
| | Female | 169 | 7.8 |
| Race | White | 1470 | 67.5 |
| | Nonwhite | 709 | 32.5 |
| Employee type | Hourly | 1900 | 87.2 |
| | Salaried | 279 | 12.8 |
| Year of hire | Before 1970 | 414 | 19.0 |
| | 1970–1979 | 681 | 31.3 |
| | 1980–1989 | 596 | 27.4 |
| | 1990–1999 | 488 | 22.4 |
| Age at hire (yr) | <20.0 | 258 | 11.8 |
| | 20.0–29.9 | 1066 | 48.9 |
| | 30.0–39.9 | 546 | 25.1 |
| | 40.0–49.9 | 248 | 11.4 |
| | 50.0+ | 61 | 2.8 |
| | Average age = 29.0 yr | | |
| Length of employment (yr) | <15.0 | 1424 | 65.4 |
| | 15.0–24.9 | 322 | 14.8 |
| | 25.0–34.9 | 282 | 12.9 |
| | 35.0+ | 151 | 6.9 |
| | Average length = 12.5 yr | | |
| Vital status (31 December 2001) | Alive | 1886 | 86.6 |
| | Dead | 293 | 13.4 |

**TABLE 2**
Cause-Specific Mortality of All Cohort Members at 11 Wood-Treating Plants

| Cause of Death | Observed | Expected | SMR | 95% CI Lower | 95% CI Upper |
|---|---|---|---|---|---|
| All causes | 293 | 325.37 | 90.1 | 80.0 | 101.0 |
| All malignant neoplasms | 90 | 84.05 | 107.1 | 86.1 | 131.6 |
| Cancer of buccal cavity and pharynx | 0 | 2.39 | 0.0 | 0.0 | 154.4 |
| Cancer of digestive organs and peritoneum | 19 | 20.21 | 94.0 | 56.6 | 146.8 |
| Cancer of esophagus | 2 | 3.25 | 61.6 | 7.5 | 222.6 |
| Cancer of stomach | 2 | 3.05 | 65.6 | 7.9 | 237.1 |
| Cancer of large intestine | 7 | 6.48 | 108.1 | 43.4 | 222.7 |
| Cancer of rectum | 2 | 1.28 | 156.1 | 18.9 | 563.9 |
| Cancer of biliary passages and liver | 2 | 2.40 | 83.3 | 10.1 | 300.9 |
| Cancer of pancreas | 4 | 3.93 | 101.7 | 27.7 | 260.4 |
| Cancer of all other digestive organs | 0 | 0.43 | 0.0 | 0.0 | 866.4 |
| Cancer of respiratory system | 40 | 30.96 | 129.2 | 92.3 | 175.9 |
| Cancer of larynx | 2 | 1.22 | 163.8 | 19.8 | 591.6 |
| Cancer of bronchus, trachea, and lung | 38 | 29.46 | 129.0 | 91.3 | 177.0 |
| Cancer of breast | 2 | 0.94 | 213.6 | 25.9 | 771.8 |
| Cancer of cervix uteri | 1 | 0.11 | 926.7 | 23.2 | 5163.7 |
| Cancer of prostate | 6 | 7.53 | 79.7 | 29.2 | 173.4 |
| Cancer of testes and other male genital organs | 0 | 0.21 | 0.0 | 0.0 | 1795.6 |
| Cancer of kidney | 3 | 1.87 | 160.5 | 33.1 | 469.1 |
| Cancer of bladder and other urinary organs | 0 | 1.44 | 0.0 | 0.0 | 256.2 |
| Malignant melanoma of skin | 1 | 1.03 | 96.6 | 2.4 | 538.5 |
| Cancer of central nervous system | 0 | 1.92 | 0.0 | 0.0 | 192.4 |
| Cancer of lymphatic and hematopoietic tissues | 13 | 7.21 | 180.3 | 96.0 | 308.4 |
| Lymphosarcoma and reticulosarcoma | 1 | 0.34 | 293.8 | 7.3 | 1637.2 |
| Hodgkin disease | 0 | 0.35 | 0.0 | 0.0 | 1041.9 |
| Leukemia | 5 | 2.63 | 190.4 | 61.8 | 444.3 |
| Cancer of other lymphopoietic tissue | 7 | 3.89 | 180.0 | 72.4 | 370.9 |
| Benign neoplasms | 2 | 0.74 | 269.8 | 32.6 | 974.7 |
| Diabetes mellitus | 3 | 7.03 | 42.7 | 8.8 | 124.8 |
| Cerebrovascular disease | 14 | 15.65 | 89.4 | 48.9 | 150.1 |
| All heart diseases | 88 | 96.29 | 91.4 | 73.3 | 112.6 |
| Ischemic heart disease | 52 | 71.65 | 72.6* | 54.2 | 95.2 |
| Chronic endocardial disease | 5 | 4.34 | 115.1 | 37.4 | 268.5 |
| Hypertension with heart disease | 2 | 4.84 | 41.4 | 5.0 | 149.4 |
| All other heart diseases | 29 | 24.91 | 116.4 | 78.0 | 167.2 |
| Hypertension without heart disease | 2 | 1.17 | 170.6 | 20.6 | 616.4 |
| Nonmalignant respiratory diseases | 19 | 21.21 | 89.6 | 53.9 | 139.9 |
| Influenza and pneumonia | 4 | 8.02 | 49.9 | 13.6 | 127.7 |
| Bronchitis, emphysema, and asthma | 0 | 3.14 | 0.0 | 0.0 | 117.4 |
| Other nonmalignant respiratory disease | 14 | 10.60 | 132.1 | 72.2 | 221.7 |
| Cirrhosis of liver | 6 | 7.79 | 77.0 | 28.3 | 167.6 |
| All external causes of death | 37 | 38.33 | 96.5 | 68.0 | 133.1 |
| Accidents | 23 | 20.69 | 111.2 | 70.5 | 166.8 |
| Motor vehicle accidents | 15 | 9.79 | 153.2 | 85.8 | 252.7 |
| All other accidents | 8 | 11.02 | 72.6 | 31.3 | 143.0 |
| Suicides | 5 | 7.69 | 65.0 | 21.1 | 151.6 |
| Homicides and other external causes | 9 | 9.95 | 90.5 | 41.4 | 171.8 |

Number of employees = 2179 person-yr = 36317.2.
*Significant at the 5% level.
CI indicates confidence interval; SMR, standardized morality ratio.

cer deaths was 90 versus 84.05 expected (SMR = 107.1, 95% CI = 86.1–131.6). No significant increase was reported for any site-specific cancer in Table 2. A nonsignificant mortality increase of approximately 30% was reported for lung cancer (SMR = 129.0, 95% CI = 91.3–177.0, 38 observed deaths). Nonsignificant mortality excesses were also reported for leukemia (five deaths) and cancer of other lymphopoietic tissue (seven deaths). As discussed here, the category "cancer of other lymphopoietic tissue" includes both NHL and MM. A separate analysis specific to NHL and MM is presented.

Mortality from a number of cancer sites was similar to expected (cancers of the digestive system, esoph-

agus, stomach, large intestine, biliary passages and liver, pancreas, prostate, and melanoma of the skin). Furthermore, no deaths were reported for several cancer sites (cancers of the buccal cavity and pharynx, other digestive organs, testes and other male genital organs, bladder and other urinary organs, central nervous system, and Hodgkin lymphoma). However, it must be noted that the numbers of expected death for some of these cancer sites were small.

For nonmalignant diseases, no significant increase was observed for any cause. In particular, a significant mortality deficit was reported for ischemic heart disease (52 observed vs. 71.65 expected, SMR = 72.6, 95% CI = 54.2–95.2), and a small

**TABLE 3**
Cause-Specific Mortality of Hourly Employees at 11 Wood-Treating Plants

| Cause of Death | Observed | Expected | SMR | 95% CI Lower | 95% CI Upper |
|---|---|---|---|---|---|
| All causes | 260 | 287.77 | 90.4 | 79.7 | 102.0 |
| All malignant neoplasms | 79 | 72.43 | 109.1 | 86.4 | 135.9 |
| Cancer of buccal cavity and pharynx | 0 | 2.14 | 0.0 | 0.0 | 172.5 |
| Cancer of digestive organs and peritoneum | 18 | 17.68 | 101.8 | 60.3 | 160.9 |
| Cancer of esophagus | 2 | 2.93 | 68.3 | 8.3 | 246.9 |
| Cancer of stomach | 2 | 2.72 | 73.5 | 8.9 | 265.5 |
| Cancer of large intestine | 6 | 5.56 | 107.8 | 39.6 | 234.7 |
| Cancer of rectum | 2 | 1.10 | 181.2 | 21.9 | 654.6 |
| Cancer of biliary passages and liver | 2 | 2.13 | 94.1 | 11.4 | 340.0 |
| Cancer of pancreas | 4 | 3.39 | 117.9 | 32.1 | 301.8 |
| Cancer of all other digestive organs | 0 | 0.37 | 0.0 | 0.0 | 1005.4 |
| Cancer of respiratory system | 36 | 26.76 | 134.5 | 94.2 | 186.2 |
| Cancer of larynx | 2 | 1.09 | 183.3 | 22.2 | 662.2 |
| Cancer of bronchus, trachea, and lung | 34 | 25.43 | 133.7 | 92.6 | 186.8 |
| Cancer of breast | 0 | 0.35 | 0.0 | 0.0 | 1062.4 |
| Cancer of cervix uteri | 0 | 0.04 | 0.0 | 0.0 | 9948.2 |
| Cancer of prostate | 6 | 6.83 | 87.9 | 32.3 | 191.3 |
| Cancer of testes and other male genital organs | 0 | 0.19 | 0.0 | 0.0 | 1980.8 |
| Cancer of kidney | 3 | 1.60 | 188.0 | 38.8 | 549.4 |
| Cancer of bladder and other urinary organs | 0 | 1.24 | 0.0 | 0.0 | 297.0 |
| Malignant melanoma of skin | 1 | 0.84 | 118.4 | 3.0 | 659.6 |
| Cancer of central nervous system | 0 | 1.60 | 0.0 | 0.0 | 230.9 |
| Cancer of lymphatic and hematopoietic tissues | 10 | 6.20 | 161.4 | 77.4 | 296.8 |
| Lymphosarcoma and reticulosarcoma | 1 | 0.29 | 345.1 | 8.6 | 1922.7 |
| Hodgkin disease | 0 | 0.31 | 0.0 | 0.0 | 1191.4 |
| Leukemia | 3 | 2.25 | 133.2 | 27.5 | 389.2 |
| Cancer of other lymphopoietic tissue | 6 | 3.35 | 179.4 | 65.8 | 390.4 |
| Benign neoplasms | 1 | 0.64 | 155.3 | 3.9 | 865.3 |
| Diabetes mellitus | 2 | 6.19 | 32.3 | 3.9 | 116.8 |
| Cerebrovascular disease | 13 | 14.04 | 92.6 | 49.3 | 158.4 |
| All heart diseases | 81 | 84.60 | 95.7 | 76.0 | 119.0 |
| Ischemic heart disease | 47 | 62.25 | 75.5 | 55.5 | 100.4 |
| Chronic endocardial disease | 5 | 3.86 | 129.6 | 42.1 | 302.5 |
| Hypertension with heart disease | 2 | 4.45 | 44.9 | 5.4 | 162.4 |
| All other heart diseases | 27 | 22.28 | 121.2 | 79.9 | 176.3 |
| Hypertension without heart disease | 2 | 1.07 | 186.6 | 22.6 | 674.1 |
| Nonmalignant respiratory diseases | 15 | 18.58 | 80.7 | 45.2 | 133.2 |
| Influenza and pneumonia | 2 | 7.25 | 27.6* | 3.3 | 99.6 |
| Bronchitis, emphysema, and asthma | 0 | 2.69 | 0.0 | 0.0 | 137.2 |
| Other nonmalignant respiratory disease | 12 | 9.13 | 131.4 | 67.9 | 229.5 |
| Cirrhosis of liver | 5 | 6.90 | 72.4 | 23.5 | 169.1 |
| All external causes of death | 35 | 35.13 | 99.6 | 69.4 | 138.6 |
| Accidents | 21 | 18.85 | 111.4 | 69.0 | 170.3 |
| Motor vehicle accidents | 14 | 8.88 | 157.6 | 86.2 | 264.5 |
| All other accidents | 7 | 10.08 | 69.5 | 27.9 | 143.1 |
| Suicides | 5 | 6.83 | 73.2 | 23.8 | 170.9 |
| Homicides and other external causes | 9 | 9.45 | 95.2 | 43.5 | 180.8 |

Number of employees = 1900 person-yr = 31551.6.
*Significant at the 5% level.
CI indicates confidence interval; SMR, standardized mortality ratio.

nonsignificant deficit was reported for nonmalignant respiratory disease (19 observed vs. 21.21 expected, SMR = 89.6, 95% CI = 53.9–139.9). On the other hand, mortality from motor vehicle accidents was elevated, but the increase was not statistically significant (SMR = 153.2, 95% CI = 85.8–252.7).

There were 279 salaried employees in the cohort. Among them, 11 died from cancer, comparable to the 11.62 expected. The cancer sites (n) were: large intestinal cancer (1), lung cancer (4), breast cancer (2), cervix uteri (1), acute lymphatic leukemia (1), acute myeloid leukemia (1), and multiple myeloma (1). No significant increase from any cancer site was found among salaried employees. However, it must be noted that the numbers of death were small.

Because most hourly workers were involved in production and maintenance, their potential for exposure was generally much higher than that of salaried employees. Additional detailed cohort analyses were conducted for hourly workers. Table 3 shows the cause-specific mortality of the 1900 hourly employees, which was quite similar to that for the entire cohort, because 87.2% of the cohort members were hourly employees. There were 260 deaths reported among hourly employees,

**TABLE 4**
Cause-Specific Mortality of Hourly Employees at 11 Wood-Treating Plants by Length of Employment

| | <15.0 Yr | | 15.0–24.9 Yr | | 25.0–34.9 Yr | | ≥35.0 Yr | |
|---|---|---|---|---|---|---|---|---|
| **Cause of Death** | **OBS** | **SMR** | **OBS** | **SMR** | **OBS** | **SMR** | **OBS** | **SMR** |
| All causes | 119 | 96.2 | 66 | 91.1 | 50 | 90.6 | 25 | 68.5 |
| All malignant neoplasms | 26 | 100.7 | 22 | 110.5 | 21 | 133.2 | 10 | 91.6 |
| Cancer of digestive organs and peritoneum | 11 | 176.6 | 4 | 81.8 | 3 | 77.1 | 0 | 0.0 |
| Cancer of esophagus | 2 | 192.1 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Cancer of stomach | 1 | 104.5 | 0 | 0.0 | 1 | 169.6 | 0 | 0.0 |
| Cancer of large intestine | 4 | 210.5 | 2 | 129.9 | 0 | 0.0 | 0 | 0.0 |
| Cancer of rectum | 0 | 0.0 | 1 | 332.2 | 1 | 414.4 | 0 | 0.0 |
| Cancer of biliary passages and liver | 1 | 126.4 | 0 | 0.0 | 1 | 221.7 | 0 | 0.0 |
| Cancer of pancreas | 3 | 254.4 | 1 | 105.9 | 0 | 0.0 | 0 | 0.0 |
| Cancer of respiratory system | 12 | 131.6 | 7 | 92.6 | 11 | 182.7 | 6 | 147.5 |
| Cancer of larynx | 1 | 257.9 | 0 | 0.0 | 1 | 410.6 | 0 | 0.0 |
| Cancer of bronchus, trachea, and lung | 11 | 127.5 | 7 | 97.4 | 10 | 174.5 | 6 | 154.4 |
| Cancer of prostate | 0 | 0.0 | 3 | 154.8 | 2 | 118.4 | 1 | 64.8 |
| Cancer of kidney | 1 | 163.7 | 1 | 230.6 | 0 | 0.0 | 1 | 469.3 |
| Malignant melanoma of skin | 1 | 222.8 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Cancer of lymphatic and hematopoietic tissues | 1 | 37.9 | 5 | 317.2* | 2 | 167.7 | 2 | 254.2 |
| Lymphosarcoma and reticulosarcoma | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 | 3627.7 |
| Leukemia | 0 | 0.0 | 2 | 352.8 | 0 | 0.0 | 1 | 349.0 |
| Cancer of other lymphopoietic tissue | 1 | 74.9 | 3 | 341.7 | 2 | 295.2 | 0 | 0.0 |
| Benign neoplasms | 1 | 363.8 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Diabetes mellitus | 1 | 42.9 | 1 | 60.8 | 0 | 0.0 | 0 | 0.0 |
| Cerebrovascular disease | 3 | 62.0 | 3 | 79.1 | 4 | 126.3 | 3 | 134.2 |
| All heart diseases | 40 | 133.7 | 13 | 56.1* | 18 | 94.9 | 10 | 79.7 |
| Ischemic heart disease | 21 | 98.0 | 8 | 46.4* | 12 | 84.0 | 6 | 64.7 |
| Chronic endocardial disease | 4 | 330.6 | 1 | 95.9 | 0 | 0.0 | 0 | 0.0 |
| Hypertension with heart disease | 1 | 59.2 | 0 | 0.0 | 1 | 108.7 | 0 | 0.0 |
| All other heart diseases | 14 | 167.8 | 4 | 67.1 | 5 | 105.6 | 4 | 123.3 |
| Hypertension without heart disease | 1 | 263.8 | 1 | 345.8 | 0 | 0.0 | 0 | 0.0 |
| Nonmalignant respiratory diseases | 3 | 49.2 | 9 | 177.3 | 3 | 69.9 | 0 | 0.0 |
| Influenza and pneumonia | 0 | 0.0 | 0 | 0.0 | 2 | 120.4 | 0 | 0.0 |
| Other nonmalignant respiratory disease | 2 | 71.8 | 9 | 348.4† | 1 | 46.5 | 0 | 0.0 |
| Cirrhosis of liver | 2 | 55.0 | 2 | 115.9 | 0 | 0.0 | 1 | 206.0 |
| All external causes of death | 27 | 105.4 | 6 | 108.3 | 1 | 36.7 | 1 | 79.2 |
| Accidents | 16 | 121.5 | 4 | 126.9 | 1 | 59.2 | 0 | 0.0 |
| Motor vehicle accidents | 10 | 149.8 | 3 | 233.4 | 1 | 157.8 | 0 | 0.0 |
| All other accidents | 6 | 91.5 | 1 | 52.9 | 0 | 0.0 | 0 | 0.0 |
| Suicides | 5 | 100.4 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Homicides and other external causes | 6 | 80.5 | 2 | 151.9 | 0 | 0.0 | 1 | 527.2 |
| Number of employees | 1723 | | 541 | | 336 | | 108 | |
| Person-yr | 22,847.9 | | 5154.9 | | 2509.2 | | 1039.6 | |

*Significant at the 5% level.
†Significant at the 1% level.
OBS indicates observed; SMR, standardized mortality ratio.

representing 88.7% of all deaths in the cohort. Similar to the total cohort, there was a 10% overall mortality deficit and there was no significant mortality increase from any cause of death among hourly employees, except for MM (see discussion subsequently).

Table 4 shows the cause-specific mortality of the hourly employees by length of employment at the wood-treating plants. There appeared to be a downward trend for mortality from all causes of death, with the SMR declining from 96.2 for <15.0 years of employment to 68.5 for ≥35.0 years of employment. The trend, however, was not statistically significant ($\chi^2$ trend = 1.19). For mortality from digestive cancers, there was a not non-significant excess among those with <15.0 years of employment, whereas non-significant deficits were reported for groups with longer employment. For mortality from lung cancer, none of the length-of-employment groups showed a significant increase, and there appeared to be no apparent pattern with respect to length of employment ($\chi^2$ trend = 0.55). There was a significant mortality increase from the broad category "all lymphatic and hematopoietic cancers" among hourly workers with 15.0–24.9 years of employment, but not in any other length-of-employment groups. Furthermore, there was no upward trend of mortality from "all lymphatic and hematopoietic cancers" in relation to length of employment ($\chi^2$ trend = 2.25). This broad category represents a heterogeneous group of cancers, including NHL, leukemia, and MM deaths. A more specific analysis for NHL, leukemia, and MM is provided below. A significant deficit was observed for heart disease (SMR = 56.1, 95% CI = 29.9–96.0) among hourly workers with 15.0–24.9 years of employment. On the other hand, a significant mortality increase from other nonmalignant respiratory disease (SMR = 348.4) was reported among hourly workers with 15.0–24.9 years of employment, but no increase was found for other length-of-employment groups, including those with more than 25 years of employment.

Table 5 shows mortality analysis by interval since hire (latency) for hourly employees. For lung cancer, the highest SMR was reported during the first 15 years after hire, but the SMR of 154.8 based on seven deaths was not statistically significant. For cancer of other lymphopoietic tissue, the highest SMR was reported for the 25.0- to 34.9-year latency group, but the SMR was based on only two deaths and not significant. The category "cancer of other lymphopoietic tissue" includes primarily NHL and MM. As stated in the previous section, a separate analysis of lymphatic and hematopoietic cancers based on a biologically meaningful classification is presented subsequently. The latency analysis in Table 5 indicates that no cause-specific SMR showed a significant increase, regardless of the length of latent period, except for mortality from motor vehicle accidents in the 15.0- to 24.9-year latency group (SMR = 297.3, six observed deaths).

The specific categories of lymphatic and hematopoietic cancers used in the OCMAP program are based on the statistical classifications compiled by National Center for Health Statistics (NCHS) and do not permit a specific analysis of major cell type-specific leukemias, NHL, or MM, which are more appropriate classifications from the biologic point of view.[9–11,17–19] Therefore, analyses of these specific subcategories of lymphatic and hematopoietic cancers were carried out separately.

Table 6 shows that there was one death from NHL (more specifically, lymphosarcoma and reticulosarcoma, ICD 200) among hourly employees, and the expected was 2.42 (SMR = 41.2, 95% CI = 1.0–229.8). All six deaths in the category "cancer of other lymphopoietic tissue" were MM (ICD 203), significantly higher than the 1.50 expected (SMR = 401.1, 95% CI = 147.2–873.1). There was one observed death from chronic lymphatic leukemia, compared with 0.37 expected (SMR = 269.2, 95% CI = 6.7–1499.9). In addition, there were two deaths from acute myeloid leukemia, compared with 0.71 expected (SMR = 283.5; 95% CI = 34.3–1024.2). On the other hand, there was no death reported for acute lymphatic leukemia or chronic myeloid leukemia.

Table 7 shows mortality from MM of hourly employees by length of employment and latency. The highest SMR was observed among employees with 15.0–24.9 years of employment. The SMRs (95% CI) were 206.1 (5.2–1148.4), 717.5 (148.1–2096.9), 588.9 (71.3–2127.3), and 0.0 (0.0–1459.0) for length of employment of <15.0, 15.0–24.9, 25.0–34.9, and ≥35.0 years. The SMRs of MM by length of employment did not show any pattern, and a formal analysis demonstrated that there was no upward trend ($\chi^2$ trend = 0.08). Analysis of mortality from MM by time since first employment (latency) is also presented in Table 7. The SMRs of MM in all latency categories were elevated, but none of the SMRs were statistically significant.

## Nested Case–Control Study

Table 8 shows the results of multivariate conditional logistic regression analyses of lung cancer mortality. Independent variables in the multivariate model included tobacco consumption, length of employment, and job/exposure categories. Table 8 shows, for each independent variable, the estimated parameter β in the regression and its standard error (SE). The OR for each independent variable can be estimated as follows: OR = exp(β). The results from the multivariate analyses showed that lung cancer risk for tobacco consumption was elevated (OR = 4.92, chi-square = 2.566, $P = 0.109$), but the OR did not reach statistical significance at the 5% level. Neither length of employment nor any job/exposure category was found to be

**TABLE 5**
Cause-Specific Mortality of Hourly Employees at 11 Wood-Treating Plants by Latency

| | <15.0 Yr | | 15.0–24.9 Yr | | 25.0–34.9 Yr | | ≥35.0 Yr | |
|---|---|---|---|---|---|---|---|---|
| **Cause of Death** | **OBS** | **SMR** | **OBS** | **SMR** | **OBS** | **SMR** | **OBS** | **SMR** |
| All causes | 63 | 82.0 | 83 | 101.2 | 65 | 98.7 | 49 | 77.6 |
| All malignant neoplasms | 16 | 116.0 | 22 | 102.6 | 22 | 112.9 | 19 | 107.3 |
| Cancer of digestive organs and peritoneum | 6 | 182.0 | 6 | 113.2 | 4 | 83.7 | 2 | 46.5 |
| Cancer of esophagus | 0 | 0.0 | 1 | 105.8 | 1 | 127.2 | 0 | 0.0 |
| Cancer of stomach | 0 | 0.0 | 1 | 125.1 | 1 | 137.9 | 0 | 0.0 |
| Cancer of large intestine | 3 | 314.7 | 2 | 125.3 | 0 | 0.0 | 1 | 67.3 |
| Cancer of rectum | 0 | 0.0 | 1 | 300.3 | 1 | 341.7 | 0 | 0.0 |
| Cancer of biliary passages and liver | 1 | 236.4 | 0 | 0.0 | 0 | 0.0 | 1 | 206.1 |
| Cancer of pancreas | 2 | 329.3 | 1 | 97.9 | 1 | 107.3 | 0 | 0.0 |
| Cancer of respiratory system | 7 | 145.8 | 9 | 109.6 | 11 | 147.8 | 9 | 142.8 |
| Cancer of larynx | 0 | 0.0 | 1 | 284.0 | 1 | 337.6 | 0 | 0.0 |
| Cancer of bronchus, trachea, and lung | 7 | 154.8 | 8 | 102.7 | 10 | 141.1 | 9 | 149.2 |
| Cancer of prostate | 0 | 0.0 | 3 | 204.9 | 0 | 0.0 | 3 | 108.7 |
| Cancer of kidney | 1 | 302.8 | 1 | 199.8 | 0 | 0.0 | 1 | 290.3 |
| Malignant melanoma of skin | 1 | 343.7 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Cancer of lymphatic and hematopoietic tissues | 1 | 63.4 | 3 | 166.1 | 3 | 202.4 | 3 | 225.5 |
| Lymphosarcoma and reticulosarcoma | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 | 2225.8 |
| Leukemia | 0 | 0.0 | 1 | 157.8 | 1 | 189.0 | 1 | 200.5 |
| Cancer of other lymphopoietic tissue | 1 | 138.5 | 2 | 198.8 | 2 | 233.3 | 1 | 131.7 |
| Benign neoplasms | 1 | 596.7 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Diabetes mellitus | 0 | 0.0 | 1 | 55.1 | 1 | 61.1 | 0 | 0.0 |
| Cerebrovascular disease | 1 | 39.8 | 4 | 106.6 | 4 | 109.2 | 4 | 97.3 |
| All heart diseases | 15 | 93.3 | 29 | 119.9 | 18 | 81.6 | 19 | 85.4 |
| Ischemic heart disease | 7 | 61.9 | 15 | 84.9 | 11 | 66.8 | 14 | 83.3 |
| Chronic endocardial disease | 2 | 363.1 | 2 | 214.4 | 0 | 0.0 | 1 | 75.0 |
| Hypertension with heart disease | 0 | 0.0 | 1 | 72.2 | 1 | 88.7 | 0 | 0.0 |
| All other heart diseases | 6 | 129.2 | 11 | 168.1 | 6 | 106.1 | 4 | 73.6 |
| Hypertension without heart disease | 0 | 0.0 | 2 | 662.8 | 0 | 0.0 | 0 | 0.0 |
| Nonmalignant respiratory diseases | 1 | 33.8 | 4 | 85.4 | 7 | 140.3 | 3 | 50.4 |
| Influenza and pneumonia | 0 | 0.0 | 0 | 0.0 | 2 | 111.6 | 0 | 0.0 |
| Other nonmalignant respiratory disease | 1 | 81.8 | 3 | 129.9 | 5 | 192.4 | 3 | 99.8 |
| Cirrhosis of liver | 0 | 0.0 | 3 | 123.2 | 1 | 78.6 | 1 | 144.7 |
| All external causes of death | 20 | 94.5 | 11 | 126.5 | 3 | 91.5 | 1 | 50.2 |
| Accidents | 11 | 102.6 | 8 | 168.3 | 2 | 99.2 | 0 | 0.0 |
| Motor vehicle accidents | 7 | 124.0 | 6 | 297.3* | 1 | 128.6 | 0 | 0.0 |
| All other accidents | 4 | 78.2 | 2 | 72.2 | 1 | 79.6 | 0 | 0.0 |
| Suicides | 3 | 74.7 | 1 | 56.7 | 1 | 149.1 | 0 | 0.0 |
| Homicides and other external causes | 6 | 93.4 | 2 | 91.7 | 0 | 0.0 | 1 | 397.6 |
| Number of employees | 1722 | | 1183 | | 541 | | 208 | |
| Person-yr | 18,317.7 | | 8584.1 | | 3134.6 | | 1515.1 | |

*Significant at the 5% level.
OBS indicates observed; SMR, standardized mortality ratio.

associated with lung cancer mortality (all ORs close to or below 1.00, chi-square less than 1.00, and *P* values considerably higher than 0.05). For example, the OR for routine exposure to creosote-based wood preservatives, after adjusting for tobacco consumption, was 0.58 (95% CI = 0.11–3.03) with chi-square = 0.423 and *P* = 0.516. Thus, the multivariate analyses of lung cancer, taking tobacco consumption and exposure variables simultaneously into consideration, demonstrated that lung cancer risk was not associated with employment at the wood-treating plants or related to exposure to creosote-based wood preservatives or creosote-treated products.

Table 9 shows the multivariate conditional logistic regression analyses of MM mortality in the case–control study. Because there were only seven MM deaths (one in salaried and six in hourly employees), in the analyses of job/exposure categories, the numbers in some categories were zero or extremely small. As a result, estimates of parameter β in the regression were extremely unstable and the corresponding SEs very large. Nevertheless, the chi-square and the *P* values can be used to evaluate the association between MM and the independent variables (tobacco consumption, length of employment, job/exposure categories). As Table 9 shows, all chi-squares were extremely small and all *P* val-

**TABLE 6**
Mortality From Non-Hodgkin Lymphoma, Multiple Myeloma, and Leukemia Among Hourly Employees

| Causes of Death | Observed | Expected | SMR | 95% CI Lower | 95% CI Upper |
|---|---|---|---|---|---|
| Non-Hodgkin lymphoma | 1 | 2.42 | 41.2 | 1.0 | 229.8 |
| Multiple myeloma | 6 | 1.50 | 401.1† | 147.2 | 873.1 |
| Leukemia | 3 | 2.25 | 133.2 | 27.5 | 389.2 |
| Acute lymphatic leukemia | 0 | 0.12 | 0.0 | 0.0 | 2959.3 |
| Chronic lymphatic leukemia | 1 | 0.37 | 269.2 | 6.7 | 1499.9 |
| Acute myeloid leukemia | 2 | 0.71 | 283.5 | 34.3 | 1024.2 |
| Chronic myeloid leukemia | 0 | 0.39 | 0.0 | 0.0 | 934.6 |

†Significant at the 1% level.
CI indicates confidence interval; SMR, standardized mortality ratio.

ues were considerably above 0.05, indicating that there was no association between MM and any of the independent variables.

## Discussion

The size of workforce at most wood-treating facilities is relatively small, compared with some other industrial operations. Because of its decentralized nature, a reasonable cohort of sufficient statistical power would require the participation of many locations. Included in the cohort were 11 wood-treating plants with a total of 2179 employees. This investigation is the largest cohort of workers exposed to creosote-based wood preservatives and/or creosote-treated wood products. The only other cohort study consisted of 922 creosote-exposed impregnators at 13 plants in Sweden and Norway. Even so, for some diseases, the statistical power of the present investigation in detecting a modest increase was still limited. Of the 2179 employees included in the cohort, 293 were identified to have died. For some causes of death, only a few deaths occurred, and results based on small numbers must be interpreted with caution.

The employees at the 11 wood-treating facilities experienced a lower overall mortality when compared with the general population in the United States. The observed 10% overall mortality deficit was consistent with the so-called "healthy worker effort" (HWE), which refers to the observation that in most occupational cohort mortality studies, the overall mortality of the cohort is lower than that of the general population. Possible explanations for the HWE include selection of health or health attributes at the time of hire, being healthy enough to hold a job, access to medical care as a benefit of employment and stable lifestyle associated with employment. The overall mortality deficit appeared to have

**TABLE 7**
Mortality From Multiple Myeloma Among Hourly Employees by Length of Employment and Latency

| Analysis | Parameter | <15.0 Yr | 15.0–24.9 Yr | 25.0–34.9 Yr | ≥35.0 Yr |
|---|---|---|---|---|---|
| Length of employment | Observed deaths | 1 | 3 | 2 | 0 |
| | Expected deaths | 0.49 | 0.42 | 0.34 | 0.25 |
| | SMR | 206.1 | 717.5* | 588.9 | 0.0 |
| | 95% CI | 5.2–1148.4 | 148.1–2096.9 | 71.3–2127.3 | 0.0–1459.0 |
| Latency | Observed deaths | 1 | 2 | 2 | 1 |
| | Expected deaths | 0.24 | 0.43 | 0.43 | 0.40 |
| | SMR | 422.3 | 464.9 | 468.9 | 248.6 |
| | 95% CI | 10.6–2353.0 | 56.2–1679.3 | 56.7–1694.1 | 6.2–1385.3 |

*Significant at the 5% level.
SMR indicates standardized mortality ratio; CI, confidence interval.

**TABLE 8**
Multivariate Conditional Logistic Regression Analyses of Lung Cancer Mortality

| Variable | β | SE(β) | Odds Ratio | 95% CI | Chi-square | *P* Value |
|---|---|---|---|---|---|---|
| Tobacco consumption | 1.59298 | 0.99444 | 4.92 | 0.70–34.54 | 2.566 | 0.109 |
| Length of employment (yr) | 0.01713 | 0.01836 | 1.01 | 0.98–1.05 | 0.871 | 0.351 |
| Routine exposure to creosote preservatives | −0.55013 | 0.84603 | 0.58 | 0.11–3.03 | 0.423 | 0.516 |
| Routine exposure to creosote-treated products | 0.37221 | 0.83852 | 1.45 | 0.28–7.51 | 0.197 | 0.657 |
| Intermittent exposure to preservatives or treated products | −0.66854 | 0.75665 | 0.51 | 0.12–2.26 | 0.781 | 0.377 |
| Intermittent exposure to treated or untreated materials | −0.79621 | 0.98813 | 0.45 | 0.07–3.13 | 0.649 | 0.420 |

CI indicates confidence interval.

**TABLE 9**
Multivariate Conditional Logistic Regression Analyses of Multiple Myeloma Mortality

| Variable | Chi-square | *P* Value |
|---|---|---|
| Tobacco consumption | 0.002 | 0.966 |
| Length of employment (yr) | 0.097 | 0.756 |
| Routine exposure to creosote preservatives | 0.000 | 0.998 |
| Routine exposure to creosote-treated products | 0.000 | 0.997 |
| Intermittent exposure to preservatives or treated products | 0.000 | 0.998 |
| Intermittent exposure to treated or untreated materials | 0.000 | 0.998 |

come primarily from ischemic heart disease (SMR = 72.6, $P < 0.05$). There was no significant increase in mortality from any particular cancer site, except for MM (more discussion of MM subsequently). In particular, there was no increase in mortality from cancer of the digestive system, prostate cancer, NHL, or malignant melanoma of the skin. Furthermore, there were no deaths from testicular cancer, bladder cancer, cancer of the central nervous system, and Hodgkin lymphoma.

Close to 90% of the cohort members were hourly workers, whose opportunities for exposures were generally much higher than those of salaried employees. A separate analysis was carried out for hourly workers. The results of the hourly workers were quite similar to those of the entire cohort. In particular, none of the cause-specific SMRs was significantly elevated, except for MM. There were six MM deaths, compared with 1.50 expected (SMR = 401.1, 95% CI = 147.2–873.1). When the data were analyzed by length of employment, no upward trend for any cause of death was detected. For example, the lung cancer SMRs among hourly workers did not show any pattern with length of employment ($\chi^2$ trend = 0.55). Although there was a significant increase of MM mortality overall, analysis by length of employment indicated that the SMR was highest among those with the 15.0–24.9 years of employment but no death in the longest length of employment group (≥35.0 years). The SMRs for MM did not show any trend ($\chi^2$ trend = 0.08). The absence of any upward trend in site-specific cancer mortality lends further support to the interpretation that there was no relation between employment at the wood-treating plants and the risk of developing cancer. Thus, the cohort analyses did not provide any evidence that employees at the 11 wood-treating plants were at an increased risk of cancer as a result of their employment or exposures at the plants.

With regard to nonmalignant diseases, no significant increases were detected in the cohort. Most of the deficit in overall mortality for the cohort could be attributed to a significant reduction in mortality from ischemic heart disease (SMR = 72.6, $P < 0.05$). Similarly, among hourly employees, the SMR for ischemic heart disease was 75.5 ($P \approx 0.05$). Analysis by length of employment did not reveal any upward trends in mortality from nonmalignant diseases. The cohort analyses demonstrate that employees at the 11 wood-treating plants did not experience any mortality increases from nonmalignant diseases as a result of their employment.

As discussed subsequently, potential limitations of the cohort analyses included the lack of information on tobacco consumption and detailed exposure. In the nested case–control study, such information was collected. As expected, tobacco consumption was found to be associated with an elevated lung cancer risk (OR = 4.92, chi-square = 2.566, $P = 0.109$), although the increased risk did not reach statistical significance at the 5% level. Length of employment was found not to be related to lung cancer mortality. The nested case–control analyses of lung cancer in terms of job/exposure categories did not reveal any association between employment in these categories and lung cancer risk, lending further support to the finding of no association between employment and lung cancer in the cohort study. Similar nested case–control analyses were performed for MM. Although the numbers were small, the analyses did not reveal any evidence that MM was related to exposure to creosote-based wood preservatives or to creosote-treated products.

We now discuss our results in conjunction with findings from previous studies reviewed earlier in this report. Of the studies reviewed, all but one were population-based (or hospital-based) case–control studies. Information on occupation in this population-based case–control was obtained from self-reported questionnaires (ie, recalls) and was subject to recall bias and inaccuracy. These studies usually did not provide information about the nature of exposure or details of employment comparable to that in cohort-based studies. Exposure classification could be highly heterogeneous even within a single population-based case–control study, and length of employment is usually not available. Furthermore, publication bias is common in such population-based case–control studies (ie, only increased risks are reported). In commenting on population-based case–control studies, the International Agency for Research on Cancer[20] stated: "Caution should also be applied in interpreting the findings from those case–control studies conducted within the general population setting. Most of the studies reported had positive findings, and are likely to be an incomplete selection of case–control studies in which occupational exposures have been investigated." Thus, methodologically speaking, cohort studies and cohort-

based or nested case–control investigations (such as the current investigation) are superior to population-based case–control studies.

From Sweden, Flodin et al[1] reported a significant OR of MM for exposure to creosote. As discussed in the literature review, the Flodin et al[1] study suffered from a number of limitations, including incomplete case ascertainment, incomparability between cases and controls, potential reporting bias, and overly broad exposure classification. For example, electrical linemen were considered to be exposed to creosote, although the only source of exposure for electrical linemen would be utility poles previously (regardless of how long ago) treated with preservatives (not necessarily creosote-based). Even Flodin et al labeled such exposure "relatively low-grade." Given these limitations, the validity of the result of the Flodin et al[1] study was questionable. On the contrary, in another Swedish case–control study, Eriksson and Karlsson[5] reported no association between creosote exposure and MM.

In comparison to population-based case–control studies, the employment and exposure information in our cohort study and cohort-based case–control analyses is by far more accurate, because it was based on documented sources: the study subjects' employment and personnel records. Furthermore, the exposure information in the case–control analyses was more specific, because exposure pattern was taken into consideration in developing the exposure categories. Because of the availability of detailed employment histories and exposure information, analyses by length of employment as well as by specific job/exposure categories were feasible. The results from our cohort study and the nested case–control analyses did not support a causal association between MM and employment at the wood-treating plants or exposure to creosote-based wood preservatives.

In another Swedish population-based case–control study, Persson et al[3] reported a nonsignificant increase of NHL in relation to creosote exposure. The Persson et al study used the same methodological approach and shared some of the controls as in the Flodin et al[1] study. As such, the Persson et al study suffered from many of the same limitations as the Flodin et al[1] investigation. In addition, the NHL result in the Persson et al[3] study was based on extremely small number of exposed subjects—only one control was exposed. Even Persson et al[3] questioned the low frequency of exposure among the controls. The authors commented: "There remains apparently the possibility that exposure to creosote for some reason has been underestimated among the referents in common." Thus, the result from the Persson et al study must be interpreted with caution.

From the United States, based on a large-scale population-based case–control study, Blair et al[6] reported no increased risk of NHL for the exposure category "asphalt and creosote." Although the numbers of exposed cases and controls were much larger (53 cases and 105 controls), the exposure category was not restricted to creosote only.

In our investigation, there was only one death from NHL, whereas 2.42 were expected. The result did not provide any evidence for a relation between exposure to creosote preservatives and NHL in our cohort.

Finally, Karlehagen et al[4] reported an increased incidence of both melanoma and nonmelanoma skin cancer in a cohort of 922 creosote impregnators in Sweden and Norway. Contrary to the population-based case–control studies conducted in Sweden, the exposure classification in the Karlehagen et al[4] cohort study appeared to be accurate because it was based on personnel records. Unfortunately, the skin cancer results were internally inconsistent between workers in Sweden and Norway and potentially confounded by concomitant exposures. The authors themselves attributed the skin cancer excess to a combination of exposures to creosote and sunlight.

In our cohort, there was one death from melanoma skin cancer, comparable to the 1.03 expected. Thus, there was no evidence that the employees at the 11 wood-treating plants experienced an increased mortality risk of melanoma skin cancer. However, the small sample size did not permit a definite conclusion. In addition, mortality may not be a sensitive end point for nonfatal nonmelanoma skin cancer.

Several potential limitations of our retrospective cohort study should be pointed out and discussed. Most of these limitations are typical of historical cohort mortality studies in general. Being a mortality study, analyses were based on the underlying cause of death listed on death certificates. As such, the study not only inherited some of the problems usually associated with death certificates (diagnostic accuracy, for example), but also suffered from the lack of in-depth clinical information. No detailed clinical information was available on the deaths in our study. However, it must be pointed out that although detailed information derived from medical records or pathology reports may be more accurate than that based on death certificates, it would be inappropriate to use such information for comparisons with national mortality rates. In our study, we compared diagnoses based on death certificates with national statistics that were derived from death certificates as well. Furthermore, our analysis was adjusted for calendar time, thus at least partially controlling for changes in survival and diagnostic practices.

The type of analysis (eg, disease categories) in the cohort study was primarily dictated by the statistical classifications of mortality rates for the U.S. population published by the National Center for Health Statistics, which were used in the OCMAP program. The statistical classifica-

tions in the OCMAP program may not always coincide with the latest understanding of disease mechanisms or the latest disease classifications. To correct this shortcoming of the OCMAP program, specific analyses were conducted for several cancer sites (NHL, MM, and subtype of leukemia).

As in most historical cohort studies, little or no quantitative exposure data were available for workers who were exposed in the 1940s or 1950s, and analyses by quantitative exposure indices were not possible. In the cohort study, we relied on duration of employment as a measure for potential exposure to creosote-based wood preservatives and creosote-treated products. In the nested case–control study of lung cancer and MM, in addition to length of employment, five detailed exposure categories based on the pattern and frequency of exposure were used.

Similarly, information on lifestyle or exposures from employment elsewhere was not available in the cohort study. For lung cancer and MM, however, histories of tobacco consumption among the study subjects were collected and incorporated in the nested case–control analyses. As such, the analyses of lung cancer and MM in the nested case–control study were adjusted for potential confounding resulting from tobacco consumption.

Finally, as stated earlier, although the cohort consisted of all workers who had ever worked at the 11 participating wood-treating plants between 1979 and 1999 and the study is the largest cohort of workers exposed to creosote, the sample size was still relatively small for certain analyses. Some analyses presented in this report lacked adequate statistical power, as in the case of several specific cancer sites. Furthermore, when analyses were stratified by length of employment, latency, or job/exposure category, the numbers of workers became even smaller, which rendered some of the stratified analyses statistically unstable. As a result, the corresponding 95% CIs were wide and the findings must be interpreted with caution. However, for common disease categories such as all cancers, digestive cancer, lung cancer, heart diseases, and nonmalignant respiratory disease, the statistical power of the study was adequate.

## Conclusion

The retrospective cohort study reported an overall favorable mortality experience of employees at the 11 participating wood-treating plants. Detailed analyses by length of employment did not reveal any upward trend of cause-specific morality. In particular, there was no association between employment at the plants and lung cancer, as demonstrated by the length-of-employment analysis in the cohort study and the analysis by job/exposure category in the nested case–control study. Although there was a statistically significant excess of multiple myeloma, the absence of an upward trend in mortality by length of employment in the cohort study and the lack of any association between job/exposure categories and multiple myeloma in the nested case–control study argued against the interpretation that the overall multiple myeloma excess was associated with employment at the plants or related to exposure to creosote-based wood preservatives and/or creosote-treated products. The investigation indicated that the employees did not experience any cause-specific mortality increase as a result of their exposure. Some of the results of the investigation, however, should be interpreted with caution, because they were based on relatively small numbers. In summary, based on the findings of the present investigation and results reported in the literature, it was concluded that employment at the 11 wood-treating plants or exposure to creosote-based wood preservatives was not associated with any significant mortality increase from either site-specific cancers or nonmalignant diseases.

## Acknowledgments

The authors are grateful to the National Death Index (NDI) of the National Center for Health Statistics for providing vital status information, to Robert Bilgrad at NDI for his valuable assistance, to state health departments for providing death certificate information, and to Koppers Inc. for sponsoring the project.

## References

1. Flodin U, Fredriksson M, Persson B. Multiple myeloma and engine exhausts, fresh wood, and creosote: a case-referent study. *Am J Ind Med*. 1987;12:519–529.
2. Flodin U, Fredriksson M, Persson B, et al. Chronic lymphatic leukemia and engine exhausts, fresh wood, and DDT: a case-referent study. *Br J Ind Med*. 1988; 45:33–38.
3. Persson B, Dahlander AM, Fredriksson M, et al. Malignant lymphomas and occupational exposures. *Br J Ind Med*. 1989;46:516–520.
4. Karlehagen S, Andersen A, Ohlson CG. Cancer incidence among creosote-exposed workers. *Scand J Work Environ Health*. 1992;18:26–29.
5. Eriksson M, Karlsson M. Occupational and other environmental factors and multiple myeloma: a population based case-control study. *Br J Ind Med*. 1992;49: 95–103.
6. Blair A, Linos A, Stewart PA, et al. Evaluation of risks for non-Hodgkin's lymphoma by occupation and industry exposures from a case–control study. *Am J Ind Med*. 1993;23:301–312.
7. Marsh GM, Youk AO, Stone RA, et al. OCMAP-Plus: a program for the comprehensive analysis of occupational cohort data. *J Occup Environ Med*. 1988;40: 351–362.
8. Breslow NE, Day NE. *Statistical Methods in Cancer Research, Volume II—The Design and Analysis of Cohort Studies*. IARC Scientific Publications No. 82. Lyon: International Agency for Research on Cancer; 1987.
9. Wong O, Raabe GK. Cell-type specific leukemia analyses in a combined cohort of more than 208,000 petroleum workers in the United States and the United Kingdom, 1937–1989. *Regul Toxicol Pharmacol*. 1995;21:307–321.
10. Wong O, Raabe GK. Multiple myeloma and benzene exposure in a multi-national cohort of more than 250,000 petroleum workers. *Regul Toxicol Pharmacol*. 1997;26:188–199.
11. Wong O, Raabe GK. Non-Hodgkin's lymphoma and exposure to benzene in a multinational cohort of more than

308,000 petroleum workers, 1937–1996. *J Occup Environ Med*. 2000;42: 554–568.
12. Young JL, Perry CL, Asire AJ. *Surveillance, Epidemiology, and End Results: Incidence and Mortality Data.* NIH Publication No. 81-2300. National Cancer Institute; 1981.
13. Selvin S, Levin LI, Merrill DW, et al. Selected epidemiologic observations of cell-specific leukemia mortality in the United States, 1969–1977. *Am J Epidemiol*. 1983;117:140–152.
14. Reis LAG, Miller BA, Hankey BF, et al. *SEER Cancer Statistics Review, 1973–1991.* NIH Publication No. 94-2789. National Cancer Institute; 1994.
15. Flickinger CW, Lawrence AW. *Occupational Health Experience in the Wood-Preserving Industry*. Bethesda, MD: American Wood-Preservers' Association; 1982.
16. SAS Institute Inc. *SAS Procedures Guide*, version 8. Gary, NC: SAS Institute Inc; 1999.
17. Linet MS. *The Leukemias: Epidemiologic Aspects.* Oxford University Press; 1985.
18. Heath CW. The leukemias. In: Schottenfeld D, Fraumeni JF, eds. *Cancer Epidemiology and Prevention*. Philadelphia: WB Saunders; 1982.
19. Wintrobe MM, Lee GR, Boggs DR, et al. *Clinical Hematology,* 8th ed. Philadelphia: Lea & Febiger; 1981.
20. International Agency for Research on Cancer. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Occupational Exposures in Petroleum Refining; Crude Oil and Major Petroleum Fuels*, vol 45. Geneva: World Health Organization; 1989.