Environmental Health Perspectives Supplements
101 (Suppl. 6): 63–76 (1993)

Health Effects of Gasoline Exposure. II. Mortality Patterns of Distribution Workers in the United States

by Otto Wong,[1] Fran Harris,[2] and Thomas J. Smith[3]

In this study, the cohort consisted of 18,135 distribution employees with potential exposure to gasoline for at least one year at land-based terminals (n = 9,026) or on marine vessels (n = 9,109) between 1946 and 1985. The primary objective of the study was to determine the relationship, if any, between exposure to gasoline and mortality from kidney cancer or leukemia. In addition, other causes of death of secondary interest included multiple myeloma and heart diseases. The mortality of the cohort was observed through June 30, 1989. The results of this study indicated that there was no increased mortality from either kidney cancer or leukemia among marketing and marine distribution employees who were exposed to gasoline in the petroleum industry when compared to the general population. Among the land-based terminal employees, the kidney cancer standardized mortality ratio (SMR) was 65.4 (12 deaths) and leukemia SMR was 89.1 (27 deaths). For the marine cohort, the SMRs were 83.7 for kidney cancer (12 deaths) and 70.0 for leukemia (16 deaths), respectively. More importantly, based on internal comparisons, there was no association between mortality from kidney cancer or leukemia and various indices of gasoline exposure. In particular, neither duration of employment, duration of exposure, age at first exposure, year of first of exposure, job category, cumulative exposure, frequency of peak exposures, nor average intensity of exposure had any effect on kidney cancer or leukemia mortality. For acute myeloid leukemia, a nonsignificant mortality increase was found in land-based terminal employees (SMR = 150.5, 13 deaths), but no trend was detected when the data were analyzed by various gasoline exposure indices. This nonsignificant excess was limited to land-based terminal employees hired before 1948. On the other hand, a deficit of mortality from acute myeloid leukemia was observed among marine employees (SMR = 74.2, 5 deaths). For the two cohorts combined, SMR for acute myeloid leukemia was 117.1 based on 18 deaths. We did not find any relationship in our study between gasoline exposure and mortality from multiple myeloma or heart diseases. In general, we did not find any significantly increased mortality, either overall or from specific causes, associated with gasoline exposure in this study of marketing and marine distribution employees.

Introduction

Some recent epidemiologic studies (*1–3*) and animal toxicologic experiments (*4*) suggested that exposure to gasoline vapors may be related to an increased risk for kidney cancer. However, other epidemiologic studies failed to find any association between gasoline exposure and kidney cancer (*5,6*). A meta-analysis based on all available studies in the petroleum industry indicated that for the industry as a whole, kidney cancer mortality was similar to that in the general population (*7*). Because gasoline contains benzene, a known leukemogen (*8–10*), leukemia is also a potential health concern. A small increased risk for multiple myeloma in petroleum distribution employees has also been reported (*1,2*). In addition, one study suggested an increased mortality from heart diseases in distribution workers (*1*).

Concerned with the potential health effects of gasoline, the American Petroleum Industry (API) decided to sponsor additional animal studies as well as epidemiologic research. In terms of epidemiologic research, API funded both a case–control study of kidney cancer among refinery workers (*6*) and an epidemiologic study of distribution/marketing workers exposed to gasoline in 1984. The distribution worker study is the subject of this report.

Before the mortality study of distribution workers, a feasibility phase was carried out in 1984–1985 to assess the availability of data (*11*). It was determined that a retrospective cohort of distribution employees exposed to gasoline could be identified through employment records. For the most part, data could be collected at a limited number

[1]Applied Health Sciences, 181 Second Avenue, Suite 628, P.O. Box 2078, San Mateo, CA 94401.
[2]ENSR Health Sciences, 1320 Harbor Bay Parkway, Suite 100, Alameda, CA 94501.
[3]Environmental Health Division, Department of Family and Community Medicine, University of Massachusetts Medical Center, 55 Lake Avenue North, Worcester, MA 01655.
Address reprint requests to O. Wong, Applied Health Sciences, 181 Second Avenue, Suite 628, P.O. Box 2078, San Mateo, CA 94401.
This manuscript was presented at the International Symposium on the Health Effects of Gasoline held 5–8 November 1991 in Miami, FL.

of centralized record retention locations (as opposed to collecting data at every terminal). The quality of available employment records appeared to be adequate for a mortality study. Work histories in terms of processes and job titles could be reconstructed and most likely could be coded according to a common scheme. Historical industrial hygiene data were limited to the mid-1970s or later, and numerical exposure quantification for earlier periods could be based on estimates. Smoking histories were not available from employment records. Verification of cohort completeness would be feasible for only certain (more recent) time periods.

The last three findings listed above (namely, inadequate historical industrial hygiene data, lack of smoking history from employment records, and inadequate documents for verification of cohort completeness) were judged to be the principal limitations of the data. The potential impact of the inadequacy of historical industrial hygiene data would be that quantitative exposure classification of the early part of the study would be based on estimates rather than on actual measurements. Although smoking data were not available directly from employment records, some information on smoking habits or smoking policy might be available for certain portions of the cohort. As such, confounding due to smoking, if any, could be addressed. Finally, the fact that it might not be feasible or practical to verify cohort completeness for the entire study period might not have any real impact on the mortality study per se, other than that the data should be examined for indirect evidence of any potential selection bias in cohort assembly.

Materials and Methods

The cohort was defined as distribution employees with potential exposure to gasoline for at least 1 year at land-based terminals or on marine vessels between 1946 and 1985 at one or more of the selected locations (terminals, regions, or divisions) or on one or more of the selected vessels. Employment records at the participating units (land-based terminals, regions, or divisions; or shipping companies) must be either complete since the start date of the unit, or retrievable for at least 20 years. These land-based terminals, regions, or divisions and marine vessels were selected based on considerations of completeness of employment records, type of products, and available length of follow-up period. The study thus consisted of two separate cohorts: marketing employees at land-based terminals and marine distribution employees. Although the exposure patterns in these two groups were somewhat different, both cohorts were exposed primarily to gasoline vapors. Four companies contributed data to the study.

It should be pointed out that gasoline distribution is only one of the functions of the marketing division, which also includes retail sales (batteries, tires, etc.) and service stations. As such, this study is more exposure-specific than other studies based on the entire marketing or distribution division. It should also be pointed out that in addition to gasoline, these distribution employees may also be exposed to other hydrocarbons and, in the case of marine employees, to crude oil as well.

The objective of the study was to determine the mortality patterns of land-based marketing and marine distribution workers with potential exposure to gasoline. In particular, the *a priori* causes of death included both leukemia and kidney cancer. Causes of death of secondary interest included multiple myeloma and heart diseases.

Typically the data collection team went to facilities where employment records of the selected locations were kept. Because of the decentralized nature of the operation, the data collection team went to more than 30 record locations for data collection. At each location, data collection was preceded by a presentation of a short overview of the study to the local company contacts, who were asked to identify the appropriate job titles and work locations or departments with potential exposure to downstream gasoline.

In general, the record centers functioned as regional record storage locations for personnel files covering all types of marketing employees. These personnel records were filed together, usually in alphabetical order. Therefore, the files had to be screened before being microfilmed. For record screening purposes, the company contacts were encouraged to provide the data collection team with a loose and liberal definition of gasoline exposure.

In parallel, an independent study was conducted to characterize the exposure patterns of the cohort (*12*). The final cohort could be identified only after all employment records had been computerized, and job titles and locations with potential exposure identified based on the parallel exposure assessment study. It should be emphasized that the procedure of data entry of work history, exposure assessment, and cohort identification was an interactive process. Figure 1 outlines the sequence of the cohort identification procedure.

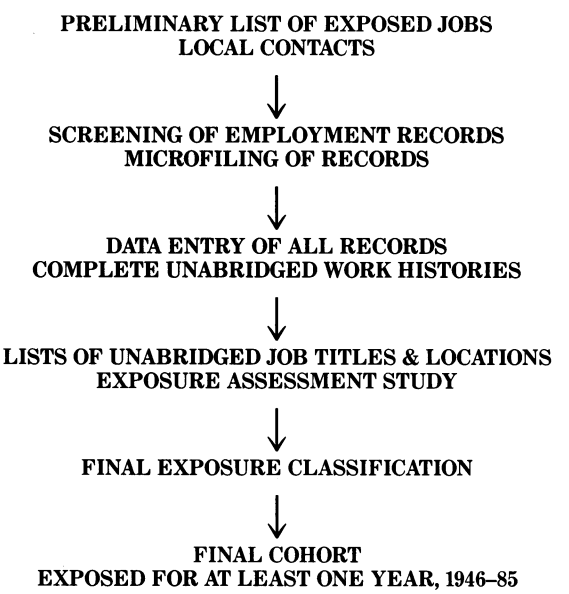

FIGURE 1. Cohort identification process.

Data collection (microfilming of employment records) took approximately 2 years to complete, and a total of approximately 68,000 employment records were microfilmed. From these employment records, basic demographic and work history information was entered into the database. The summary work history consisted of, in chronological order, a list of jobs, along with the corresponding work locations or facilities, as well as the corresponding dates. Listings of job titles and work locations or facilities encountered in data entry were generated to aid the parallel exposure assessment study. The listings consisted of approximately 6100 job titles, 4800 land-based terminal and other locations, and 3000 vessels. The coded data in the database underwent extensive editing and checking. Any errors detected during this coding check were corrected and documented. Error rates from the data check were 1.2% for both demographic variables and work history.

Ideally, cohort verification provides an independent means of assessing *a*) whether or not a cohort is complete and *b*) if the cohort is incomplete, whether that would result in any systematic bias. We concluded in our feasibility report that a complete cohort verification was not possible in this population. Various methods for conducting a systematic, comprehensive cohort verification were proposed and rejected as being impractical. Because of the decentralized nature of the cohort, verification of completeness through the use of Social Security quarterly reports (941 forms) was not viable. The possibility of using workers' compensation records for cohort verification was also investigated. Unfortunately, there were no job titles in workers' compensation records, and these records were incomplete and not easily retrievable. API also met with the Coast Guard to investigate the feasibility of using the Coast Guard's Shipping Articles. Subsequently, API reported that it appeared impractical to use the Coast Guard's data.

Even though no comprehensive approach was feasible, several attempts were made to verify cohort completeness and the absence of systematic bias in the data. These attempts included checking the cohort against lists of deaths among distribution workers known to the companies, names of co-workers based on recalls of retired long-term employees, as well as additional names from a variety of documents such as company newsletters and memoranda. These investigations did not provide any evidence that a major selective removal of records was ever a practice at any of the companies.

The vital status of the cohort was determined through the following sources. As coding of basic information was completed, records were sent to the Social Security Administration (SSA) for vital status follow-up. The majority of the land-based terminal cohort was submitted to SSA before SSA's policy change in 1988 of discontinuing its service in vital status ascertainment. To supplement the SSA follow-up, the remaining cohort as well as those unknown to SSA were checked against the Death Master File (DMF; a database of 39 million deaths in the United States since 1937) and the National Death Index (NDI; a national mortality registry since 1979). In addition, companies were also asked to provide any vital status information available on cohort members. Based on information provided by SSA, DMF, NDI, or the participating companies, appropriate state vital statistics departments were contacted for copies of death certificates. A nosologist coded the primary cause of death, plus up to three contributing causes, for all death certificates received. The 8th Revision of the International Classification of Diseases (ICD) was used.

A parallel study of exposure assessment among the cohort members was conducted, and detailed results of the study have been reported separately (*12*). Concentration of total hydrocarbons in parts per million (ppm) was used as a measure of exposure to individual components in gasoline. In all epidemiologic analyses, exposure concentrations refer to total hydrocarbons. In characterizing job activities of land-based terminal employees, four generic job categories were created based on exposure patterns or proximity to sources: drivers, loaders, terminal operators, and other terminal jobs. All job titles encountered in employment records in the study were then assigned to one of the above generic categories. A time-weighted average (TWA) exposure matrix was calculated for these job categories in each of the four time periods (<1950, 1950–64, 1965–74, 1975–86) for the land-based terminal operations. A similar process was followed for the marine operations. Two generic job categories (deck and nondeck) were created. Time-weighted average exposures by time period (<1980, 1980–85) were estimated for deck personnel on inland waterway barges only. There were not enough data to estimate seagoing tanker personnel exposures.

In our epidemiologic analyses, two quantitative exposure indices were used: cumulative exposure and peak exposure. Cumulative exposure was defined as the sum of products of TWA exposure and duration of exposure of each job in an employee's work history. The unit of cumulative exposure was in ppm-years. In our study, cumulative exposure ranged from 2 to 8000 ppm-years. In general, long-term drivers at small terminals had the highest exposures, and short-term workers with "other terminal jobs" had the lowest.

In this study, a peak exposure was defined as an episode of exposure in excess of 500 ppm lasting 15–90 minutes. The annual frequency of peak exposures for each job was determined by identifying the tasks with the potential to produce peaks and estimating the annual number of occurrences of these tasks. For each subject, a lifetime frequency of peak exposures was calculated. Lifetime cumulative frequency of peak exposures in our study ranged from 0 to 24,000. Drivers at small terminals had the highest number of peak exposures because of the high frequency of peaks during loading and small deliveries. Although the peak exposures of inland waterway barge deck personnel were more intense than those of drivers, peak exposures of the former were less frequent because of the much lower loading frequency.

In addition to cumulative exposure and peak exposure, length of exposure was used in the epidemiologic analyses. For chronic diseases, a latent period precedes the appearance of symptoms. In other words, exposure imme-

diately before diagnosis is not likely to be associated with the disease. To take latency into consideration, a truncated length of exposure was created, in which any exposure within the last 10 years of observation (i.e., 10 years before death or end of study) was not counted.

Mortality analysis was based on the standardized mortality ratio (SMR). Person-years of observation began at cohort entry (1 year after first exposure, or January 1, 1947, whichever was later) and continued to the end of the study period (June 30, 1989) or the date of death, whichever was earlier. The U.S. national age-race-sex-cause-specific mortality rates of 5-year periods were applied to these person-years to obtain the number of deaths from a particular cause to be expected from an equal number of person-years of the same race and sex and similar in age and calendar year. The actual computation was carried out with the University of Pittsburgh OCMAP program (*13*).

Because death certificates were not obtained for all deaths identified, relying only on deaths with death certificates might underestimate the actual number of deaths by cause. To adjust for this, deaths without death certificates were redistributed by causes according to the cause-specific proportions among deaths with death certificates. The adjusted cause-specific SMRs and 95% confidence interval (CI) were based on these adjusted deaths. SMRs and 95% CI in all the tables, and the discussion in this report refers to these adjusted SMRs and adjusted 95% CIs.

Cause-specific SMRs were calculated separately for each of the two cohorts (land-based terminal and marine) for a variety of exposure variables. These subcohort analyses based on SMRs provided an indirect means for internal comparison. It should be pointed out that many of the exposure variables were time-related and, therefore, correlated with one another. Ideally, some analyses should be performed on data stratified by two or more of these time-related variables. However, the size of data precluded detailed stratification.

In addition to SMRs, the Cox's proportional hazards model (*14,15*) was also used in analyzing the *a priori* causes of death data: kidney cancer and leukemia. One advantage of the proportional hazards model was that the actual data (e.g., ppm-years) could be used, instead of grouping the data into several broad categories such as was done in the SMR analyses. Another advantage of the proportional hazards model was that the comparison was internal, without basing the comparison on an external comparison population, such as the case of SMRs based on a comparison to the general population. In occupational studies, the appropriateness of an external population as the basis of comparison can always be questioned, because of the healthy worker effect, the comparability of health-influencing habits, as well as the completeness of reporting. Since the proportional hazards model relied directly on internal comparison, many of these potential problems could be avoided or at least minimized.

Results

There were 9026 land-based distribution and 9109 marine distribution employees in the study. Because the majority of the cohort members were white, individuals with unknown race were assumed to be white in the analyses. Similarly, individuals with unknown sex were assumed to be male. Table 1 shows the descriptive statistics of the cohort members. The vital status of the cohort members was determined as of June 30, 1989 (Table 2).

Table 1. Descriptive statistics of land-based marketing and marine distribution employees.

Variable	Land-based	Marine
Number	9,026	9,109
Person-years	239,125	227,134
Sex		
Male	8,768	8,719
Female	207	99
Unknown	51	291
Race		
White	5,798	4,096
Nonwhite	475	468
Unknown	2,753	4,545
Average year of hire	1954	1950
Average year of first exposure	1957	1957
Average length of employment, years	21.1	12.2
Average length of exposure, years	17.1	5.1
Average length of follow-up, years	26.5	24.9

Table 2. Vital status as of June 30, 1989, of land-based marketing and marine distribution employees.

	Land-based		Marine	
Vital status	Number	%	Number	%
Alive	6960	77.1	6414	70.4
Deceased	2066	22.9	2695	29.6
With death certificates	2009	97.2	2295	85.2
Without death certificates	57	2.8	400	14.8

Mortality Patterns of Land-based Distribution Employees

Table 3 shows the observed deaths by cause, cause-specific SMRs, and the corresponding 95% confidence limits for the entire cohort of land-based terminal employees. The overall mortality of the cohort was only half of the expected (SMR = 51.3 based on 2066 observed deaths), the deficit being statistically significant. Mortality from all malignant neoplasms was also significantly lower than the expected based on the U.S. general population (SMR = 66.4, 520 observed deaths). None of the site-specific cancer SMRs showed any increase over the expected. In fact, most of the site-specific cancer SMRs were significantly low. For example, SMR for cancer of the digestive system was 69.4 ($p < 0.01$, 151 observed deaths). For lung cancer, the SMR was 66.2 ($p < 0.01$, 165 observed deaths).

For kidney cancer, one of the *a priori* causes, the observed number of deaths was 12, with an SMR of 65.4 (nonsignificant). For leukemia, the other *a priori* cause, the SMR was 89.1 (nonsignificant), based on a total of 27 deaths. Thus, for both *a priori* causes of death, there was a nonsignificant deficit in mortality. For all lymphopoietic cancer, the SMR of 75.4 was significantly lower than the

Table 3. Observed deaths by cause, standardized mortality ratios (SMRs), and 95% confidence limits for land-based terminal cohort members.[a]

Cause of death (*ICDA-8*)[b]	Observed	SMR	Lower	Upper
All causes of death (1–999)	2066	51.3**	49.1	53.6
All malignant neoplasms (140–209)	520	66.4**	60.7	72.5
Cancer of digestive organs and peritoneum (150–159)	151	69.4**	59.1	81.0
Cancer of respiratory system (160–163)	173	65.8**	56.5	76.2
Cancer of lung (162–163)	165	66.2**	56.8	76.6
Cancer of kidney (189)	12	65.4	33.7	114.1
Leukemia and aleukemia (204–207)	27	89.1	59.4	128.8
Cancer of other lymphatic tissue (202–203, 208)	18	91.9	54.4	145.1
All lymphopoietic cancer (200–209)	55	75.4*	57.5	97.0
Allergic, endocrine, metabolic, nutritional diseases (240–279)	30	44.6**	30.1	63.7
Diabetes mellitus (250)	20	35.0**	21.6	53.5
All diseases of circulatory system (390–458)	1039	48.9**	45.9	52.0
All respiratory diseases (460–519)	150	56.5**	48.1	65.9
Cirrhosis of liver (571)	31	36.5**	24.6	52.1
Motor vehicle accidents (810–827)	35	44.9**	31.2	62.5
Suicide (950–959)	26	39.4**	26.0	57.4

[a]SMRs adjusted for deaths with unknown causes.
[b]Disease code according to the *Eighth Revision of the International Classification of Diseases.*
*Significant at $p < 0.05$; **significant at $p < 0.01$.

expected (based on 55 observed deaths). Although multiple myeloma was not analyzed separately in the OCMAP program, mortality from "cancer of other lymphatic tissue," which included multiple myeloma as a major component, was as expected (SMR = 91.9, based on 18 observed deaths).

Mortality from circulatory diseases was extremely low (SMR = 48.9, 1039 observed deaths), which had a significantly favorable influence on the overall mortality. Mortality from endocrine, metabolic, and nutritional diseases as well as from diabetes mellitus was also extremely low, with SMRs of 44 . 6 ($p < 0.01$, 30 observed deaths) and 35.0 ($p < 0.01$, 20 observed deaths), respectively. For nonmalignant respiratory diseases, the SMR was 56. 5 based on 150 observed deaths ($p < 0.01$). Significantly low SMRs were also observed for cirrhosis of the liver (SMR = 36.5, $p < 0.01$, 31 observed deaths). Of particular interest to this cohort, which included a large number of professional drivers, SMR for motor vehicle accidents was significantly low (SMR = 44.9, $p < 0.01$, 35 observed deaths).

Table 4 shows the cause-specific mortality by length of exposure. No significantly elevated cause-specific SMRs were found for any category of length of exposure. Furthermore, no trend was apparent for any cause-specific mortality. For the two cancer sites of *a priori* interest, no significantly elevated SMRs were found for any of the groups by length of exposure. For those with more than 30 years of exposure, kidney cancer and leukemia SMRs were 60.8 (3 observed deaths) and 81.4 (7 observed deaths), respectively. Mortality pattern by truncated exposure was similar to that by full length of exposure and will not be reported separately.

Analysis by time since first exposure or latency is presented in Table 5. No significant excess for any causes was detected, regardless of time since first exposure. In particular, SMRs for kidney cancer and leukemia were 55.4 (6 observed deaths) and 100.2 (19 observed deaths), respectively, for the group with 30 or more years after first exposure. There appeared to be an upward trend in SMRs for all causes by time since first exposure. In the first 10 years after exposure, the overall SMR was 29.2 based on 71 observed deaths ($p < 0.01$), reaching 59.3 based on 1500 observed deaths ($p < 0.01$) after 30 or more years. Similarly, there was a slight increase of lung cancer mortality by time since first exposure. The most prominent trend, however, was that observed for mortality from circulatory diseases (SMRs ranging from 15.8 to 56.4).

Table 4. Observed deaths by cause and standardized mortality ratios (SMRs) for land-based terminal cohort members by length of exposure.[a]

	1–4 years		5–9 years		10–19 years		20–29 years		30+ years	
Cause of death (*ICDA-8*)[b]	Observed	SMR	Observed	SMR	Observed	SMR	Observed	SMR	Observed	SMR
All causes of death (1–999)	150	48.5*	145	41.6*	405	45.6*	717	53.7*	648	56.4*
All malignant neoplasms (140–209)	43	79.3	40	64.2*	113	68.1*	167	61.3*	157	69.0*
Cancer of lung (162–163)	12	71.3	18	90.2	39	73.8	55	61.8*	41	58.2*
Cancer of kidney (189)	0	–	0	–	6	146.0	3	46.9	3	60.8
Leukemia and aleukemia (204–207)	2	78.4	2	74.8	7	107.6	9	90.9	7	81.4
Cancer of other lymphatic tissue (202–203,208)	1	71.8	1	63.1	6	147.4	8	117.7	2	35.0
All diseases of circulatory system (390–458)	57	44.4*	61	39.7*	178	39.8*	377	51.4*	366	55.4*

[a]SMRs adjusted for deaths with unknown causes.
[b]Disease code according to the *Eighth Revision of the International Classification of Diseases.*
*Significant at $p < 0.01$.

Table 5. Observed deaths by cause and standardized mortality ratios (SMRs) for land-based terminal cohort members by time since first exposure.[a]

Cause of death (*ICDA-8*)[b]	<10 years		10–19 years		20–29 years		30+ years	
	Observed	SMR	Observed	SMR	Observed	SMR	Observed	SMR
All causes of death (1–999)	71	29.2**	171	33.3**	324	43.4**	1500	59.3**
All malignant neoplasms (140–209)	24	64.6*	48	52.2**	93	62.3**	355	70.7**
Cancer of lung (162–163)	6	58.1	18	59.4*	31	59.7**	110	70.6*
Cancer of kidney (189)	0	–	3	119.6	3	75.3	6	55.4
Leukemia and aleukemia (204–207)	0	–	4	104.8	4	76.8	19	100.2
Cancer of other lymphatic tissue (202–203,208)	0	–	0	–	6	167.3	12	93.7
All diseases of circulatory system (390–458)	13	15.8**	68	31.1**	139	37.9**	819	56.4**

[a]SMRs adjusted for deaths with unknown causes.
[b]Disease code according to the *Eighth Revision of the International Classification of Diseases.*
*Significant at $p < 0.05$; **significant at $p < 0.01$.

Several broad categories of jobs were defined for land-based terminal employees according to their pattern of exposure. Drivers were estimated to have higher exposure to gasoline vapors than operators and men in other terminal jobs. Table 6 shows the mortality for those terminal employees who had been drivers only, operators only, or other terminal jobs only. For the two causes of death of *a priori* interest, kidney cancer and leukemia, none of the jobs exhibited a significant excess. In fact, drivers tended to have lower mortality from both kidney cancer and leukemia than terminal operators. A similar analysis for cohort members who were ever in the above three broad job categories was performed, and similar results were obtained.

As discussed above, each exposed job was assigned an 8-hr TWA exposure to total hydrocarbons in parts per million. The assigned TWA might change according to time period. Based on these TWAs and the duration of exposure at each level, a cumulative exposure (concentration multiplied by duration) in ppm-years was calculated for each individual in the land-based terminal cohort. Table 7 presents the cause-specific mortality by level of cumulative exposure. There were no significant increases in any cause-specific mortality regardless of level of cumulative exposure. There appeared to be a slight upward trend in overall mortality by level of cumulative exposure, with the overall SMRs ranging from 43.9 to 56.6. For kidney cancer and leukemia, all the SMRs were within the expected range regardless of cumulative exposure. Furthermore, there were no trends in the SMRs for these two cancer sites by cumulative exposure.

Table 6. Observed deaths by cause and standardized mortality ratios (SMRs) for land-based terminal cohort members in only one specific generic job category.[a]

Cause of death (*ICDA-8*)[b]	Driver only		Operator only		Other terminal jobs only	
	Observed	SMR	Observed	SMR	Observed	SMR
All causes of death (1–999)	500	52.0**	197	57.0**	102	33.7**
All malignant neoplasms (140–209)	130	70.0*	56	81.9	32	52.8**
Cancer of lung (162–163)	39	65.2**	21	93.7	7	37.1**
Cancer of kidney (189)	2	45.1	1	62.2	1	71.3
Leukemia and aleukemia (204–207)	5	68.8	4	155.5	2	87.5
Cancer of other lymphatic tissue (202–203,208)	6	127.8	0	–	2	130.1
All diseases of circulatory system (390–458)	243	49.0**	101	56.8**	43	27.8**

[a]SMRs adjusted for deaths with unknown causes.
[b]Disease code according to the *Eighth Revision of the International Classification of Diseases.*
*Significant at $p < 0.05$; **significant at $p < 0.01$.

Table 7. Observed deaths by cause and standardized mortality ratios (SMRs) for land-based terminal cohort members by cumulative exposure (ppm-years).[a]

Cause of death (*ICDA-8*)[b]	<500		500–1000		1000–2000		2000+	
	Observed	SMR	Observed	SMR	Observed	SMR	Observed	SMR
All causes of death (1–999)	316	43.9**	251	47.7**	453	49.6**	1046	56.6**
All malignant neoplasms (140–209)	98	72.1**	65	61.7**	118	66.0**	239	65.9**
Cancer of lung (162–163)	31	69.7*	21	61.7*	40	69.7*	73	64.4**
Cancer of kidney (189)	4	118.7	1	39.5	4	94.7	3	36.5
Leukemia and aleukemia (204–207)	5	88.4	3	73.3	7	103.5	12	87.3
Cancer of other lymphatic tissue (202–203,208)	4	111.9	2	75.5	4	90.3	8	89.6
All diseases of circulatory system (390–458)	124	38.6**	123	44.1**	224	45.9**	568	54.8**

[a]SMRs adjusted for deaths with unknown causes.
[b]Disease code according to the *Eighth Revision of the International Classification of Diseases.*
*Significant at $p < 0.05$; **significant at $p < 0.01$.

Table 8. Observed deaths by cause and standardized mortality ratios (SMRs) for land-based terminal cohort members by cumulative frequency of peak exposure.[a]

Cause of death (*ICDA-8*)[b]	<100		100–500		500–3000		>3000	
	Observed	SMR	Observed	SMR	Observed	SMR	Observed	SMR
All causes of death (1–999)	314	45.2*	215	53.0*	509	48.1*	1028	58.3*
All malignant neoplasms (140–209)	89	64.0*	55	69.2*	145	68.2*	231	65.7*
Cancer of lung (162–163)	21	47.5*	22	83.2	56	81.5	66	60.4*
Cancer of kidney (189)	2	58.0	1	48.7	5	97.6	4	48.4
Leukemia and aleukemia (204–207)	6	104.7	5	147.8	4	48.4	12	87.2
Cancer of other lymphatic tissue (202–203,208)	4	107.8	2	92.1	2	36.7	10	113.3
All diseases of circulatory system (390–458)	143	39.7*	100	50.3*	244	42.9*	552	55.2*

[a]SMRs adjusted for deaths with unknown causes.
[b]Disease code according to the *Eighth Revision of the International Classification of Diseases.*
*Significant at $p < 0.01$.

In addition to an 8-hr TWA, frequency of peak exposures was also determined for each exposed job. For each land-based terminal cohort member, a lifetime cumulative number of peaks was calculated. Analysis by cumulative frequency of peak exposures is given in Table 8. There were no significantly elevated cause-specific SMRs regardless of the cumulative number of peak exposures. Furthermore, there was no trend for any causes of death by cumulative frequency of peak exposures. In particular, the number of peak exposures to gasoline vapors had no influence on mortality from either kidney cancer or leukemia in this cohort of land-based terminal employees.

In addition to cause-specific SMRs, we also analyzed the data using the Cox's proportional hazards model. We limited the analysis to the two causes of death of *a priori* interest: kidney cancer and leukemia. Several independent variables were included in the models: age, race, sex, duration of exposure, cumulative exposure (ppm-years), and lifetime frequency of peak exposures to gasoline vapors. In one model, both duration of exposure and average exposure intensity were analyzed.

Table 9 shows the results of four proportional hazards models for kidney cancer and leukemia. For either kidney cancer or leukemia, the β coefficients (slopes of the regression) for duration, cumulative exposure, cumulative frequency of peak exposure, and exposure intensity were not significantly different from zero. That is, based on these Cox's proportional hazards models, exposure to gasoline vapors according to these indices exerted no influence on kidney cancer or leukemia mortality.

Most of the existing occupational epidemiologic studies do not analyze leukemia data by cell type, primarily because of the scarcity of cell-type-specific data and the difficulties in using ICD codes before the 8th revision to differentiate cell types. The OCMAP program used in our study does not analyze leukemia mortality data by cell type either. However, recent investigations demonstrate that leukemia comprises a group of several distinct malignancies with different clinical and epidemiologic features. An excellent summary of the importance of cell type specific analysis of leukemia can be found in *The Leukemias: Epidemiologic Aspects* by Linet (*16*). Several previous epidemiologic studies indicate that exposure to benzene or petroleum products containing benzene may result in an increased risk of acute myeloid leukemia but not other cell types (*10,17,18*).

In the land-based terminal cohort, the SMR for leukemia of all cell types combined was 89.1. To investigate whether there was any increase of leukemia mortality for any specific cell type among the land-based terminal employees, leukemia SMRs by cell type were calculated (Table 10). In calculating the expected deaths, age-specific leukemia rates by cell type for the United States, 1968–1977, were used (*19*). Of the four major cell types presented

Table 9. Analysis of kidney cancer and leukemia mortality based on the proportional hazards model in the land-based terminal cohort.[a]

Model and parameter	Kidney cancer		Leukemia	
Model 1				
Exposure variable	Duration		Duration	
β	0.0124012		−0.0375327	
SD	0.0334610		0.0199696	
p	0.7109		0.0602	
Model 2				
Exposure variable	Cumulative exposure		Cumulative exposure	
β	−0.0002364		−0.0000150	
SD	0.0002738		0.0001324	
p	0.3878		0.9096	
Model 3				
Exposure variable	Peak exposure		Peak exposure	
β	0.0000350		0.0000117	
SD	0.0000775		0.0000414	
p	0.6510		0.7777	
Model 4				
Exposure variable	Duration	Intensity	Duration	Intensity
β	0.0108032	−0.0091998	−0.0383784	0.0031910
SD	0.0332362	0.0077748	0.0201213	0.0039282
p	0.7451	0.2367	0.0565	0.4166

[a]In all four models, the following variables are always in the model: age, race, and sex.

Table 10. Analysis of leukemia mortality by cell type among land-based terminal employees exposed to gasoline vapors.

Cell type	Observed	SMR	95% Confidence interval
Acute lymphocytic	2	125.9	15.2–454.5
Chronic lymphocytic	2	34.7	4.2–125.2
Acute myeloid	13	150.5	80.0–257.2
Chronic myeloid	1	25.8	0.6–143.3

SMR, standardized mortality ratio.

in Table 10, only acute myeloid leukemia (AML) showed an increase. The AML SMR was 150.5 based on 13 deaths, with a 95% CI from 80.0 to 257.2 and did not reach statistical significance ($\chi^2 = 2.21, p = 0.14$). The numbers of deaths for other cell types were small, and no excess was detected.

For AML, an analysis based on the Cox's proportional hazards model was also performed. The relationship between AML mortality and gasoline exposure was assessed with respect to the following variables: duration of exposure, cumulative exposure, lifetime frequency of peak exposures, and average exposure intensity. None of these exposure variables showed a relationship with AML mortality.

Mortality Patterns of Marine Distribution Employees

Table 11 shows the observed deaths by cause, cause-specific SMRs, and the corresponding 95% confidence limits for the entire cohort of marine distribution employees. The overall SMR of the marine cohort was 76.9 (2,695 observed deaths, $p < 0.01$), and that for all malignant neoplasms was 93.3 (561 observed deaths, nonsignificant). Both the overall and all-cancer SMRs of the marine employees were typical of an industrial cohort (healthy worker effect).

Mortality from digestive cancer was significantly lower than the expected (SMR = 83.1, 138 observed deaths), whereas respiratory cancer was close to the norm (SMR = 104.6, 215 observed deaths). For the two cancers of *a priori* interest, kidney cancer and leukemia, a deficit in mortality was observed. Twelve deaths were attributed to kidney cancer, with an SMR of 83.7 (nonsignificant). For leukemia, there were 16 deaths, and the corresponding SMR was 70.0 (nonsignificant). In addition, the SMR for all lymphopoietic cancer was significantly low (60.5, $p < 0.01$, 34 observed deaths).

For nonmalignant causes of death, circulatory diseases exhibited a significantly low SMR of 64.1 based on 1024 observed deaths. Mortality from nonmalignant respiratory diseases, cirrhosis of the liver, and motor vehicle accidents was as expected.

For the entire marine cohort as a whole, there were two significantly elevated SMRs. There were two deaths from breast cancer among the marine cohort members, and the corresponding breast cancer SMR was 838.9 ($p < 0.05$). Both breast cancer decedents were male. The other significantly elevated SMR was for suicide. There were 70 deaths resulting from suicides. The corresponding SMR for suicide was 131.9 ($p < 0.05$).

Analysis by length of exposure is reported in Table 12. Because most individuals were exposed for less than 10 years, most of the deaths fell into the first two categories in Table 12. There were few deaths among those with 20 or more years of exposure. No significant cause-specific SMRs were found by length of exposure except for suicide in the 1- to 4-year group. Furthermore, no upward trend was apparent for any cause of death by length of exposure. In particular, length of exposure to gasoline vapors appeared to have no influence on mortality from kidney cancer or leukemia in this cohort of marine employees. Results based on analysis by truncated length of exposure were similar to those based on the unabridged length of exposure and will not be reported separately. In the exposure assessment study, exposure levels were estimated for deck personnel on inland waterway barges only. No estimates were provided for seagoing tanker personnel. The number of inland waterway barge employees was too small for a separate analysis. Thus, no quantitative exposure analysis (cumulative exposure or peak exposure) was performed. For the marine cohort, length of exposure to gasoline was used as a surrogate exposure index.

Table 13 shows cause-specific mortality by time since first exposure. There was no evidence of any increasing trend for any specific cancer site. For kidney cancer and

Table 11. Observed deaths by cause, standardized mortality ratios (SMRs), and 95% confidence limits for marine cohort members.[a]

Cause of death (*ICDA-8*)[b]	Observed	SMR	Lower	Upper
All causes of death (1–999)	2695	76.9**	73.9	79.9
All malignant neoplasms (140–209)	561	93.3	86.6	100.5
Cancer of digestive organs and peritoneum (150–159)	138	83.1*	70.7	96.9
Cancer of respiratory system (160–163)	215	104.6	92.0	118.4
Cancer of lung (162–163)	208	106.7	93.8	120.8
Cancer of breast (174)	2	838.9*	101.6	3028.5
Cancer of kidney (189)	12	83.7	45.8	140.5
Leukemia and aleukemia (204–207)	16	70.0	42.2	109.4
Cancer of other lymphatic tissue (202–203, 208)	11	73.3	39.0	125.3
All lymphopoietic cancer (200–209)	34	60.5**	43.2	82.5
Allergic, endocrine, metabolic, nutritional diseases (240–279)	50	97.3	74.3	125.2
Diabetes mellitus (250)	40	92.4	67.4	123.7
All diseases of circulatory system (390–458)	1024	64.1**	60.5	67.8
All respiratory diseases (460–519)	181	93.6	81.1	107.5
Cirrhosis of liver (571)	77	110.4	89.1	135.7
Motor vehicle accidents (810–827)	60	90.2	70.4	114.0
Suicide (950–959)	70	131.9*	104.7	164.3

[a]SMRs adjusted for deaths with unknown causes.
[b]Disease code according to the *Eighth Revision of the International Classification of Diseases.*
*Significant at $p < 0.05$; **significant at $p < 0.01$.

Table 12. Observed deaths by cause and standardized mortality ratios (SMRs) for marine cohort members by length of exposure.[a]

	1–4 years		5–9 years		10–19 years		20–29 years		30+ years	
Cause of death (*ICDA-8*)[b]	Observed	SMR	Observed	SMR	Observed	SMR	Observed	SMR	Observed	SMR
All causes of death (1–999)	1476	76.9**	706	77.6**	433	78.4**	71	68.0**	9	45.6*
All malignant neoplasms (140–209)	319	96.1	124	82.8*	94	97.4	20	102.2	4	130.6
Cancer of lung (162–163)	121	110.0	47	99.0	32	107.1	7	106.4	1	87.2
Cancer of kidney (189)	6	73.5	3	94.5	3	120.8	0	–	0	–
Leukemia and aleukemia (204–207)	11	87.1	3	58.7	2	48.1	0	–	0	–
Cancer of other lymphatic tissue (202–203,208)	6	71.9	2	44.5	1	36.8	2	345.0	0	–
All diseases of circulatory system (390–458)	513	60.5**	301	72.4**	175	63.9**	32	63.2**	3	34.1*
Suicide (950–959)	49	135.4*	15	140.2	6	114.1	0	–	0	–

[a]SMRs adjusted for deaths with unknown causes.
[b]Disease code according to the *Eighth Revision of the International Classification of Diseases.*
*Significant at $p < 0.05$; **significant at $p < 0.01$.

leukemia, there was no elevation of mortality in any of the time periods by time since first exposure. Furthermore, there was no trend by time since first exposure for the two causes of death of *a priori* interest. Mortality from circulatory diseases was significantly low for all four time periods in Table 13. Mortality from suicide was significantly elevated for two time periods: SMR = 165.0 ($p < 0.05$) within the first 10 years after initial exposure, and SMR = 164.6 ($p < 0.05$) in the 20- to 29-year group.

In the marine cohort, there were only two broad categories of jobs: deck and nondeck. In general, deck employees' exposures were higher than those experienced by nondeck employees. However, the mortality patterns in the two groups were quite similar (Table 14). No increased mortality was found for either kidney cancer or leukemia for either the deck or nondeck cohort members. Mortality from suicide was found to be higher than the expected among the nondeck workers (SMR = 160.5, $p < 0.05$).

Mortality among marine employees was analyzed by duration in deck jobs. For lung cancer, those with 3–4 years of deck jobs experienced an SMR of 187.0 (29 deaths, $p < 0.01$). For those with 1–2 years of deck jobs, their suicide SMR was 144.7 (46 observed, $p < 0.05$). However, no upward trend was observed for any of these causes of

Table 13. Observed deaths by cause and standardized mortality ratios (SMRs) for marine cohort members by time since first exposure.[a]

	<10 years		10–19 years		20–29 years		30+ years	
Cause of death (*ICDA-8*)[b]	Observed	SMR	Observed	SMR	Observed	SMR	Observed	SMR
All causes of death (1–999)	240	66.1**	516	69.1**	824	85.2**	1115	78.0**
All malignant neoplasms (140–209)	37	86.1	102	88.3	164	95.1	258	95.9
Cancer of lung (162–163)	15	123.6	41	109.7	58	99.4	94	108.0
Cancer of kidney (189)	0	–	3	106.8	4	100.4	5	76.2
Leukemia and aleukemia (204–207)	0	–	6	138.5	3	54.8	7	74.1
Cancer of other lymphatic tissue (202–203,208)	0	–	1	29.4	2	39.2	8	116.0
All diseases of circulatory system (390–458)	40	37.6**	158	54.4**	334	75.0**	492	64.7**
Suicide (950–959)	16	165.0*	18	121.8	22	164.6*	14	109.7

[a]SMRs adjusted for deaths with unknown causes.
[b]Disease code according to the *Eighth Revision of the International Classification of Diseases.*
*Significant at $p < 0.05$; **significant at $p < 0.01$.

Table 14. Observed deaths by cause and standardized mortality ratios (SMRs) for marine cohort members by generic job category.[a]

	Deck only		Nondeck only	
Cause of death (*ICDA-8*)[b]	Observed	SMR	Observed	SMR
All causes of death (1–999)	696	72.7**	1154	77.0**
All malignant neoplasms (140–209)	147	87.4	233	90.7
Cancer of lung (162–163)	63	111.5	69	85.3
Cancer of kidney (189)	5	124.4	4	72.3
Leukemia and aleukemia (204–207)	5	80.4	5	53.4
Cancer of other lymphatic tissue (202–203,208)	3	60.4	6	94.5
All diseases of circulatory system (390–458)	265	61.1**	458	65.3**
Suicide (950–959)	16	99.9	32	160.5*

[a]SMRs adjusted for deaths with unknown causes.
[b]Disease code according to the *Eighth Revision of the International Classification of Diseases.*
*Significant at $p < 0.05$; **significant at $p < 0.01$.

Table 15. Analysis of leukemia mortality by cell type among marine employees exposed to gasoline vapors.

Cell type	Observed	SMR	95% Confidence interval
Acute lymphocytic	1	79.5	2.0–441.6
Chronic lymphocytic	4	93.7	25.5–239.6
Acute myeloid	5	74.2	24.0–173.3
Chronic myeloid	4	132.9	36.2–339.8

SMR, standardized mortality ratio.

death. In general, there was no pattern by length of employment in deck jobs for any cause of death. In particular, length of employment in deck jobs did not seem to affect either kidney cancer or leukemia mortality.

Similar to the land-based terminal cohort, a special analysis of leukemia mortality by cell type in the marine cohort was carried. Table 15 shows the results of the leukemia cell-type analysis for the marine cohort. None of the four cell types showed a significant increase. In particular, mortality from AML was less than expected (SMR = 74.2, based on 5 observed deaths).

Discussion

In this study, unlike most previous studies in the petroleum industry, quantitative exposure estimates were made. The exposure assessment component was important to the epidemiologic study for a number of reasons. First, not all employees in the marketing or marine distribution division were exposed, and the definition of our cohort depended on exposure rather than on general employment. As such, the identification of an exposed cohort itself relied on a valid exposure classification. Second, an exposure scheme would also allow us to differentiate between various levels of exposure among study subjects within the cohort. This differentiation was important because a significant portion of our analyses was based on internal comparisons between various subcohorts by exposure. In epidemiology, one of the most important criteria in determining causation is the presence of a dose–response relationship. The exposure assessment made such a dose–response analysis possible.

Our analyses consisted of the traditional SMR approach, which relied on an external comparison to the general population. Although the SMR procedure is the most commonly used method of analysis in a cohort mortality study, there are several well-known limitations associated with this procedure, including the so-called healthy worker effect. Furthermore, the appropriateness of using the general population as the basis of comparison for every type of work or industry is certainly debatable. In a recently published article (*20*), it was demonstrated that mortality patterns were markedly different across social class, with the overall SMRs ranging from 47 to 126.

Because of the healthy worker effect as well as other reasons (discussed below), a significant portion of our analyses was based on internal comparisons between various subcohorts. Some of these internal comparisons were based on the indirectly adjusted SMRs. Although a comparison of SMRs may be criticized on theoretical grounds (*21*), the procedure is usually quite robust, provided that the same comparison population is used and the age distributions of the subcohorts are not markedly different (*8*). In addition to the SMR calculations, we also used the Cox's proportional hazards model to analyze mortality data for the two *a priori* causes of death: kidney cancer and leukemia. In our interpretation of the results, we relied heavily on internal comparisons based on both the SMR approach and the Cox's proportional hazards model.

The overall mortality was quite different between the land-based terminal and the marine cohorts. The overall SMR for the land-based cohort was 51.3 ($p < 0.01$), whereas that for the marine cohort was 76.9 ($p < 0.01$). The remarkable mortality deficit observed in the land-based terminal cohort came primarily from the following major causes of death: circulatory diseases (SMR = 48.9), nonmalignant respiratory diseases (SMR = 56.5), nonmalignant digestive diseases (SMR = 32.9), external causes of death (SMR = 37.2), and, to a lesser extent, digestive cancer (SMR = 69.4) and lung cancer (SMR = 66.2). All these cause-specific SMRs were significant at the 0.01 level.

In most occupational mortality studies, an overall mortality deficit of 20–30% is quite common. A deficit as large as 50%, however, is rarely observed. Thus, the overall SMR of 76.9 for the marine cohort was typical of an occupational study, whereas the overall SMR of 51.3 for the land-based terminal cohort was atypical. Nevertheless, SMRs of 50–60 have been reported previously (*22–27*). Table 16 presents some examples of occupational groups with low overall SMRs.

Thus, there are reports of occupational populations with a deficit of 40–50% in overall mortality. Nevertheless, in the presence of such a low overall SMR, it is important to determine whether there was any selection bias associated with the data. First, our cohort verification did not indicate any major incompleteness. In addition, we also investigated the possibility of selective (administrative) removal of records of employees based on health reasons (i.e., deaths or disabilities), as well as selective transfer of less healthy employees out of the marketing division. The investigation indicated that there was not a significant number of employment records missing, and that there was no evidence of bias introduced by missing records, even if the latter occurred. However, there was evidence that there was a certain amount of selection at the time of hire, as well as health screening and maintenance during employment, which could account partially for the low overall SMR. The upward trends observed for mortality

Table 16. Examples of low overall SMRs reported in literature.

Population	Number	SMR
Texaco pipeline field workers (*22*)	1,065	57
Texaco producing and pipeline workers (*22*)	11,098	63
Amoco salaried, white male workers (*23*)	1,984	54
Shell Deer Park chemical plant (*24*)	2,553	60
Chevon Research Center, Richmond, CA (*25*)	3,496	52
New York farm owners and operators (*26*)	18,811	65
Rocky Flat nuclear weapons plant (*27*)	5,413	62

SMR, standardized mortality ratio.

from all causes, all cancers, respiratory cancer, circulatory diseases, and nonmalignant respiratory diseases by time since first exposure or hire in the land-based cohort supported the assumption of selection at hire, which would have a diminishing effect over time.

As stated earlier, drivers are required to pass periodic physical examinations to retain their jobs. Commercial driving has long been a highly regulated occupation, even before the Department of Transportation (DOT) was formed. Prior to DOT, the Interstate Commerce Commission (ICC) was responsible for motor carrier safety regulations. For example, in 1936 ICC promulgated a set of requirements for drivers, which consisted of not only a good driving record but also "good physical and mental health," no drug addiction, and no excessive drinking (*28*). Regulations such as these would no doubt have an impact on both hiring policy and hiring practice. Furthermore, drivers are likely to be more aware of their health status and more likely to choose a lifestyle that would maintain their health. Because they are employees of large corporations, medical care would be more accessible to the land-based terminal cohort members than the general population.

The cohort definition in this study required a minimum exposure of 1 year, whereas most other studies used 6 months or 1 year of employment in their cohort definitions. The majority of the land-based distribution cohort members were long-term employees. Epidemiologic studies have demonstrated that short-term employees in some industries are frequently associated with high overall mortality (*29,30*). During our data collection, records of a large number of workers with less than 1 year of exposure were copied. To investigate the overall mortality of these workers with less than year of exposure, a 10% simple random sample was checked against the Death Master File, and overall SMRs were calculated (Table 17). The analysis indicated that, indeed, those with less than 1 year of exposure experienced an elevated overall SMR of 188.7 ($p < 0.01$). In addition, for those with less than 6 months of overall employment, the SMR was 312.6 ($p < 0.01$). Thus, the data indicated that, as a whole, the overall mortality of the entire database (eligible and ineligible study subjects) was typical of an industrial cohort. The low overall SMR in the land-based cohort was partially a reflection of the exclusion of the less healthy short-term employees.

We also examined the smoking habits among the land-based marketing employees. Many of the causes of death that showed a significant mortality deficit were tobacco related. These diagnostic categories included heart diseases, nonmalignant respiratory diseases, lung cancer, and, to a lesser extent, other cancers. The mortality deficits from these tobacco-related diseases in the land-based terminal cohort suggested that there might be an inverse confounding effect due to less cigarette smoking. That is, there were fewer smokers among the land-based terminal cohort members and/or the smokers in this cohort smoked less. This is certainly a plausible explanation because there have always been stringent restrictions on cigarette smoking in this particular industry.

Smoking data from one of the participating companies indicated that the proportion of current smokers among approximately 1400 drivers enrolled in the company's motor vehicle medical surveillance program in 1984 was 30%, lower than the 40% in the general population and considerably less than the 47% among blue collar workers (*31*). On the other hand, 41% of the marine employees of the same company were current smokers in a similar 1980 survey. Thus, the smoking pattern among marine employees was similar to that of the general population. Unfortunately, no information was available on ex-smokers for this company. A second company reported that 33% of its DOT drivers were current smokers, 10% were former smokers, and 57% never smoked. The proportion of ex-smokers in the general population was 40% and never-smokers 20% (*31*). Thus, company regulations, ad hoc surveys, and observed mortality patterns suggested that there were fewer current and former smokers among the land-based terminal employees (especially when compared to other blue collar workers).

Drinking while driving was one of the frequent grounds for dismissal. It was interesting to note that SMR for cirrhosis of the liver in the land-based terminal cohort was only 36.5 ($p < 0.01$). This result suggested the possibility that the cohort members not only smoked less but drank less as well. Epidemiologic studies have demonstrated that, in general, persons who consume less tobacco and alcohol, such as Mormons, have a much more favorable mortality pattern than the general population.

With respect to socioeconomic status, drivers have higher income and higher education than other blue collar workers in general. One of the participating companies in the study reported that 90% of drivers had a high school or higher education compared to 70% in the marine cohort, which was similar to that in refinery workers. In the general population, according to the 1980 census, only 69% have completed high school or higher education (*32*). As demonstrated in numerous studies, socioeconomic status is a major determinant of mortality (*20,33*).

In summary, we examined a variety of information to investigate the observed low overall SMR in the land-based terminal cohort. The possibility of selective removal of records of deceased employees and employees placed on medical disability was investigated. It was concluded that these records were retained in the general files and were thus accessible to the data collection team. The most likely explanations for the observed low overall mortality in the land-based cohort were selection at the time of hire, health maintenance, the exclusion from the study of workers with short-term exposure, inverse confounding due to less

Table 17. Overall mortality among ineligible land-based terminal workers who were exposed to gasoline vapors for less than 1 year.

Length of exposure	Length of employment	SMR	95% Confidence interval
<1 year	< 6 months	312.6**	218.9–432.8
<1 year	> 6 months	141.7*	102.5–190.8
<1 year	All	188.7**	149.4–235.2

SMR, standardized mortality ratio.
*Significant at $p < 0.05$; **significant at $p < 0.01$.

smoking and less drinking, and a higher socioeconomic status. It is unlikely that any single factor is responsible entirely for the observed mortality deficit. It is more likely that the observed mortality deficit in this study resulted from a combination of these factors.

The finding of the observed low overall mortality was also consistent with morbidity data collected by one of the participating companies; the overall morbidity ratio for all causes between DOT drivers and all manufacturing employees in the company was 0.65. This means that drivers are healthier than other petroleum workers, who are in turn healthier than the general population.

Regardless of the underlying reasons for the mortality deficit, there was no indication to suggest that any incompleteness of records or follow-up would correlate with classification or level of exposure. This point is important because our interpretation of the data relied heavily on analyses based on internal comparisons. Thus, the issue of whether the general population was an appropriate basis for comparison was irrelevant. Other investigators have also recommended the use of internal comparisons in analyzing occupational cohort mortality data (*34,35*).

It should also be pointed out that the mortality patterns of the marine cohort, which consisted of approximately the same number of employees as the land-based terminal cohort, was typical of an occupational study. The consistency in kidney cancer and leukemia mortality patterns between the marine and the land-based terminal cohorts further supports our interpretation of the land-based terminal cohort data.

Our analyses consisted of a series of internal comparisons within each cohort. Subcohorts were grouped according to length of exposure to gasoline, time since first exposure, broad job categories, cumulative exposure to total hydrocarbons, and cumulative frequency of peak exposures. These subcohort analyses consistently showed that there was no elevated mortality from either kidney cancer or leukemia, the two causes of death of *a priori* interest. More importantly, there was no trend by length of exposure or cumulative exposure. In fact, there was no dose–response relationship for either kidney cancer or leukemia according to any of the exposure variables.

In addition to cause-specific SMRs, the Cox's proportional hazards model was also used in our analyses. Duration of gasoline exposure, cumulative exposure, lifetime frequency of peak exposures and exposure intensity were used as exposure classification variables in four different models. None of these variables showed any relationship with either kidney cancer or leukemia. Thus, the results based on modeling were consistent with the SMR analyses.

The marine cohort data presented a similar pattern for both kidney cancer and leukemia. There was no mortality increase in either disease of *a priori* interest among the marine cohort members. Analyses by length of gasoline exposure, time since first exposure, year of first exposure, as well as by broad job categories did not identify any increased mortality from kidney cancer or leukemia. Additionally, no upward trend was detected in any of the analyses for these two diseases. A review of the original employment histories (rather than in terms of generic categories) of all kidney cancer and leukemia deaths did not reveal any clustering of specific job titles, work locations, or facilities.

Based on the results of this study, we conclude that there was no increased mortality risk for either kidney cancer or leukemia as a result of exposure to gasoline at levels similar to those experienced by workers in our study. For the combined cohort of land-based terminal and marine employees, kidney cancer SMR was 74.0 and leukemia SMR was 80.3 (Table 18).

When cell-type-specific leukemia data were analyzed, we found a nonsignificant increase of acute myeloid leukemia (AML) among the land-based terminal employees (SMR = 150.5, $p > 0.05$). No other leukemia cell type showed an increased risk. An examination of the work histories of the 13 AML cases indicated that 11 were hired before 1948, 1 in 1951, and the remaining 1 in 1974. In 1947, the recommended benzene standard (8-hr TWA) in the United States was lowered from 100 ppm to 50 ppm, and in 1948, it was further lowered to 35 ppm. Thus, it could be inferred that benzene levels in the industry in general could be relatively higher before 1948. The finding of 11 AML cases who began their employment in the industry before 1948 was consistent with this supposition. Among the marine employees there was a deficit in AML mortality (SMR = 74.4, nonsignificant). For the combined cohort of land-based terminal and marine employees, AML SMR was 117.1 (Table 18), based on 18 deaths (nonsignificant). Furthermore, with respect to exposure to gasoline, results based on proportional hazards models did not indicate any relationship between AML mortality and exposure to total hydrocarbons. Unfortunately, no estimates for benzene levels were made in the parallel exposure assessment investigation.

The two diseases of secondary interest were multiple myeloma and heart diseases. In our analyses, multiple myeloma was included as part of the diagnostic category "other lymphatic tissue cancer." None of the analyses suggested any increased mortality from other lymphatic tissue cancer in either the land-based terminal or the marine cohort. Analyses by various exposure indices did not reveal any upward trend.

For heart diseases, both the land-based terminal and the marine cohorts experienced a remarkable deficit.

Table 18. Mortality from kidney cancer and leukemia for the combined cohort of land-based terminal and marine employees exposed to gasoline.

Causes of death	Land-based terminal	Marine	Combined
Kidney cancer			
SMR	65.4	83.7	74.0
Observed deaths	12	12	24
Leukemia (all cell types)			
SMR	89.1	70.0	80.3
Observed deaths	27	16	43
Acute myeloid leukemia			
SMR	150.5	74.2	117.1
Observed deaths	13	5	18

SMR, standardized mortality ratio.

There was no suggestion in the data to imply that the employees in either cohort experienced an increased mortality from heart diseases as a result of their exposure to gasoline.

In the marine cohort as a whole, we found two cause-specific mortality excesses that were statistically significant. There were two breast cancer deaths in the marine cohort, and both were male. Although the corresponding SMR was statistically significant, no conclusion could be drawn from a finding based on only two cases. A review of the employment histories did not indicate any unusual exposure pattern. In fact, both decedents were classified as nondeck personnel, with minimal exposure. No other studies have reported breast cancer among workers exposed to gasoline. Therefore, we conclude that the two cases of breast cancer were not likely to be related to occupational exposure and represent most likely an observation by chance.

Mortality from suicide was also significantly elevated among the marine employees (SMR = 131.9). It was unlikely that this external cause of death was somehow related to gasoline exposure in this population of marine employees. Furthermore, there was no indication of any trend by duration of gasoline exposure. In fact, the suicide excess came from the group employed for 1–4 years (SMR = 207.7). This group of relatively short-term employees might have other risk factors that would increase their suicidal tendency. We did not have data on these individuals other than their employment histories at the participating companies. Thus, an investigation of the causes of the high suicide rate was beyond the scope of this study.

We would like to point out some limitations of this investigation within the context of a cohort mortality study. Because of the decentralized nature of the industry, there was much heterogeneity in personnel record-keeping. There were no documents suitable for a complete cohort verification. It is possible that some eligible employees could have been missed. However, as discussed earlier, there was no indication of selective removal of records based on health status that would introduce biases.

The retrieval of death certificates was quite successful in the land-based cohort. For the marine cohort, the number of outstanding death certificates was higher than we would prefer. In the SMR calculation, we compensated the missing death certificates by redistributing deaths without death certificates (hence, without causes of death) according to the corresponding cause-specific proportions among deaths with known causes. This procedure is commonly used to deal with missing death certificates.

On the other hand, the study had several desirable features. The observation covered a long period of time, 1946–1989. Thus, length of follow-up was quite adequate in the study. With respect to size, this study consisted of more than 18,000 exposed individuals. The statistical power of the study to detect a modest increase in mortality from the diseases of *a priori* interest was very high.

An important component of this epidemiologic investigation was the quantitative exposure assessment. In the study, a complete detailed employment history was coded for every cohort member. For each job and location encountered in the study, an exposure estimate was developed based on available industrial hygiene data and relevant facility changes. As a result of these exposure estimates, mortality analyses based on qualitative as well as quantitative exposure indices were possible. These dose–response analyses formed the basis for internal comparisons across various subcohorts by exposure. As we have emphasized above, because internal comparisons do not involve an external comparison population, our analyses and interpretation based on these internal comparisons would not be affected by the choice of an external comparison population.

Conclusion

The results of this study indicate that there was no increased mortality from either kidney cancer or leukemia among marketing and marine distribution employees in the petroleum industry, who were exposed to gasoline, when compared to the general population. Furthermore, based on internal comparisons, there was no association between mortality from kidney cancer or leukemia and various indices of gasoline exposure. In particular, neither duration of gasoline exposure, cumulative exposure, frequency of peak exposures, nor average intensity of exposure had any effect on kidney cancer or leukemia mortality.

For acute myeloid leukemia, a nonsignificant mortality increase was found in land-based terminal employees, but no trend was detected when the data were analyzed by various gasoline exposure indices. This nonsignificant excess was limited to land-based terminal employees hired before 1948. On the other hand, a deficit of mortality from acute myeloid leukemia was observed among marine employees. For the two cohorts combined, acute myeloid leukemia mortality was as expected.

We did not find any relationship in our study between gasoline exposure and mortality from multiple myeloma or heart diseases. In general, we did not find any significantly increased mortality, either overall or from specific causes, associated with gasoline exposure in this study of marketing and marine distribution employees.

We thank P. E. Enterline, M. W. First, D. H. Wagman, and T. L. Thomas for review and advice; the American Petroleum Institute OH 38-D Task Force for assistance; and the American Petroleum Institute for sponsoring the project.

REFERENCES

1. Rushton, L., and Alderson, M. R. Epidemiological survey of oil distribution centres in Britain. Br. J. Ind. Med. 40: 330–339 (1983).
2. Schnatter, A. R., Theriault, G., Katz, A. M., Thompson, F. S., Donaleski, D., and Murray, N. A retrospective mortality study within operating segments of a petroleum company. Am. J. Ind. Med. 22: 209–229 (1992).
3. Steineck, G., Plato, N., Gerhardsson, M., Norell, S. E., and Hodgstedt, C. Increased risk of urothelial cancer in Stockholm during 1985–87 after exposure to benzene and exhausts. Int. J. Cancer 45: 1012–1017 (1990).

4. MacFarland, H. N., Ulrich, C. E., Holdsworth, C. E., Kitchen, D. N., Halliwell, W. H., and Blum S. C. A chronic inhalation study with unleaded gasoline vapor. J. Am. Coll. Toxicol. 3: 231–248 (1984).
5. McLaughlin, J. K., Blot, W. J., Mehl, E. C., Stewart, P. A., Venable, F. S., and Fraumeni, J. F. Petroleum-related employment and renal cell cancer. J. Occup. Med. 27: 672–674 (1985).
6. Poole, C., Satterfield, M. H., Levin, L., Rothman, K. J., and Dreyer, N. A. A Case-Control Study of Kidney Cancer among Petroleum Refinery Workers. Technical Report submitted to American Petroleum Institute, Washington, DC, 1990.
7. Wong, O., and Raabe, G. K. Critical review of cancer epidemiology in petroleum industry employees, with a quantitative meta-analysis by cancer site. Am. J. Ind. Med. 15: 283–310 (1989).
8. Wong, O. An industry wide mortality study of chemical workers occupationally exposed to benzene. I. General results. Br. J. Ind. Med. 44: 365–381 (1987).
9. Wong, O. An industry wide mortality study of chemical workers occupationally exposed to benzene. II. Dose-response analyses. Br. J. Ind. Med. 44: 382–395 (1987).
10. Rinsky, R. A., Smith, A. B., Hornung, R., Filloon, T. G., Young, R. J., Okun, A. A., and Landrigan, P. J. Benzene and leukemia, an epidemiologic risk assessment. N. Engl. J. Med. 316: 1044–1050 (1987).
11. Wong, O., and Morgan, R. W. Feasibility Analysis for an Historical Prospective Mortality Study of Employees Exposed to Downstream Gasoline in the Petroleum Industry. Technical Report submitted to American Petroleum Institute, Washington, DC, 1985.
12. Smith, T. J., Hammond, S. K., and Wong, O. Health effects of gasoline exposure. I. Exposure assessment for U.S. distribution workers. Environ. Health Perspect. 101(suppl. 6): 13–21 (1993).
13. Marsh, G. M., and Preininger, M. OCMAP, a user-oriented occupational cohort mortality analysis program. Am. Stat. 34: 254 (1980).
14. Cox, D. R. Regression models and life tables (with discussion). J. R. Stat. Soc. 34: 187–220 (1972).
15. Breslow, N. E. Analysis of survival data under the proportional hazards model. Int. Stat. Rev. 43: 45–58 (1975).
16. Linet, M. S. The Leukemias: Epidemiologic Aspects. Oxford University Press, New York, 1985.
17. Brandt, L., Nilsson, P. G., and Mitelman, F. Occupational exposure to petroleum products in men with acute non-lymphocytic leukemia. Br. Med. J. 1: 553 (1978).
18. Wongsrichanalai, C., Delzell, E., and Cole, P. Mortality from leukemia and other diseases among workers at a petroleum refinery. J. Occup. Med. 31: 106–111 (1989).
19. Selvin, S., Levin, L. I., Merrill, D. W., and Winkelstein, W. Selected epidemiologic observations of cell-specific leukemia mortality in the United States, 1969-1977. Am. J. Epidemiol. 117: 140–152 (1983).
20. Goldblatt, P., Fox, J., and Leon, D. Mortality of employed men and women. Am. J. Ind. Med. 20: 285–306 (1991).
21. Wong, O. Further criticisms on epidemiological methodology in occupational studies. J. Occup. Med. 19: 220–222 (1975).
22. Divine, B. J., and Barron, V. Texaco mortality study: III. A cohort study of producing and pipeline workers. Am. J. Ind. Med. 11: 189–202 (1987).
23. Nelson, N. A. Mortality in AMOCO Oil Refinery Employees, Phase I. Technical Report, AMOCO Oil Company, Chicago, IL, 1985.
24. Marsh, G. M., Enterline, P. E., and McCraw, D. Mortality patterns among petroleum refinery and chemical plant workers. Am. J. Ind. Med. 19: 29–42 (1991).
25. Morgan, R. W., and Wong, O. Cause-Specific Mortality among Employees of Chevron Research Company. Technical Report submitted to Chevron, San Francisco, CA, 1983.
26. Stark, A. D., Chang, H. G., Fitzgerald, E. F., Riccadi, K., and Stone, R. R. A retrospective cohort study of mortality among New York State farm bureau members. Arch. Environ. Health 42: 204–212 (1987).
27. Wilkinson, G. S., Tietjen, G. L., Wiggs, L. D., Galke, W. A., Acquavella, J. F., Reyes, M., Voelz, G. L., and Waxweiler, R. J. Mortality among plutonium and other radiation workers at a plutonium weapons facility. Am. J. Epidemiol. 125: 231–250 (1987).
28. Interstate Commerce Commission. Motor Carrier Safety Regulations. ICC Reports Ex Parte No. MC-4, Washington, DC, 1936.
29. McDonald, A. D., Fry, J., Woolley, A. J., and McDonald, J. C. Dust exposure and mortality in an American chrysotile asbestos friction products plant. Br. J. Ind. Med. 41: 151–157 (1984).
30. Guberan, E., and Usel, M. Unusual mortality pattern among short term workers in the perfumery industry in Geneva. Br. J. Ind. Med. 44: 595–601 (1987).
31. Department of Health and Human Services. The Health Consequences of Smoking, Cancer and Chronic Lung Disease in the Workplace. U.S. Government Printing Office, Washington, DC, 1985.
32. Bureau of Census. U.S. Census of Population: 1980, Vol. 1. U.S. Government Printing Office, Washington, DC, 1985.
33. Kaplan, G. A., Haan, M. N., Syme, S. L., Minkler, M., and Winkleby, M. Socioeconomic status and health. In: Closing the Gap, the Burden of Unnecessary Illness (R. W. Amler and H. B. Dull, Ed.), Oxford University Press, New York, 1987, pp. 125–129.
34. Redmond, C. K., and Breslin, P. P. Comparison of methods for assessing occupational hazards. J. Occup. Med. 17: 313–317 (1975).
35. Alderson, M. Occupational studies – the use of national and industrial comparisons or an internal analysis. In: Quantification of Occupational Cancer, Banbury Report No. 9 (R. Peto and M. Schneideran, Eds.). Cold Spring Harbor Laboratory, Cold Springs Harbor, NY, 1981, pp. 599–608.