# Mortality from Leukemia and Other Diseases among Workers at a Petroleum Refinery

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*This study evaluates the mortality experience of 9484 white men who worked at a petroleum refinery. We compared the numbers of deaths among these men during the period 1940 through 1984 with the numbers expected on the basis of the mortality rates of US white men.* Overall, *there were 2874 observed compared with 3568 expected deaths (standardized mortality ratio, 77). Mortality rates for most major cause of death categories and most cancers were also lower than expected. However, there was a statistically significant 50% excess of leukemia deaths (44 observed/29.6 expected). Lymphocytic leukemia was increased both among men hired before 1940 and among men hired in 1940 or later. In contrast, myelocytic leukemia was increased only among men hired in 1940 or later. The restriction of the myelocytic leukemia excess to men hired in 1940 or later may be related to process changes which occurred at the refinery after 1940 and which resulted in an increased percentage of benzene in certain refinery streams. The presence of an excess of lymphocytic leukemia, but not myelocytic leukemia, among men hired before 1940 suggests that some factor other than benzene was responsible for the former condition.*

This study examines the overall and cause-specific mortality patterns of workers at a petroleum refinery in southern Illinois. The refinery started operating in 1918. Its operations now include crude oil refining and production of gasoline, diesel fuel, aviation fuel, lubricating oils, and various petrochemicals.

Both a follow-up study and a case-control study of leukemia among workers at the refinery have been done.[1,2] The follow-up study examined the cause-specific mortality experience of 3976 white men.[1] During the study period of 1973 through 1982, their mortality rates were lower than those of US white men for all causes, all cancers, and all other major disease categories. However, there was a twofold increase in leukemia mortality, based on 14 observed and 6.6 expected deaths (standardized mortality ratio (SMR) = 213; 96% confidence interval (CI) = 117 to 358). Eight of the 14 men who died of leukemia had acute myelocytic leukemia (AML) (SMR = 394, 95% CI = 172 to 788). Because benzene is present in petroleum refineries and is generally considered to be a cause of AML,[3] the observation of an excess of this disease was of particular interest and was evaluated further in a nested case-control study.[2] The latter investigation did not identify any specific job or department as responsible for the leukemia excess, and comparison of the benzene exposure levels of cases and controls did not indicate any association with benzene.

The present study further examines the mortality patterns of white men employed at the refinery. It is an expansion of the previous study in terms of both the number of workers included and the duration of the follow-up period.

## Methods

The study includes all men not known to be black (they are referred to hereafter as "white men") who met the following criteria: (1) employed at the refinery for at least 6 months before Jan 1, 1984; (2) hourly and employed on Jan 1, 1942, or later; or (3) salaried and

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employed on Jan 1, 1940, or later. We did not include hourly workers who terminated employment before 1942 or salaried workers who terminated employment before 1940 because their employment records were not routinely available.

Plant and corporate records provided the following information on each employee: name, Social Security number, company identification number, gender, race, birth date. dates of first employment and of termination at the refinery, employment status (active, retired, or terminated) and payroll classification (hourly, salaried, or both). Two mutually exclusive employee subgroups were defined on the basis of payroll classification. ''Hourly'' employees were men who had ever been hourly, including those who had started as hourly and subsequently transferred to salaried positions. "Salaried" employees were men who had never been hourly. Salaried employees were further classified as ever employed in production-related (PR) jobs or as employed only in nonproduction-related (NPR) jobs. A job was considered to be PR if it involved at least 20% of an employee's time in areas with potential exposure to refinery chemicals.

We used company, Social Security Administration (SSA) and National Death Index records to determine the vital status of the cohort members as of Jan 1, 1985. The SSA provided information on deaths occurring through 1984 and identified men presumed living as of 1983. Death certificates were obtained from the company or from state vital records offices. A nosologist coded the underlying cause of death according to the International Classification of Diseases.[4]

We compared the mortality experience of the refinery workers with that of the US general population, using the SMR as the measure of association. The *SMR* is defined as the ratio of the observed to the expected number of deaths, multiplied by 100. To obtain expected numbers of deaths, we multiplied the refinery workers' age- and calendar time-specific person-years of follow-up (grouped in 5-year categories) by the corresponding cause-specific mortality rates of US white men. For salaried workers, follow-up began 6 months after the first date of employment or on Jan 1, 1940, for men hired more than 6 months before 1940. For hourly workers, follow-up began 6 months after the first date of employment or on Jan 1, 1942, for men hired more than 6 months before 1942. Follow-up continued until death or until Jan 1, 1985. Men identified by the SSA as alive in 1983 and not reported as deceased in 1984 were assumed to have remained alive until December 31. 1984. For men lost to follow-up, person-years were accumulated up to the date of termination of employment at the refinery.

We calculated approximate 95% CI of the SMRs assuming a Poisson distribution for the observed numbers of deaths. Results are designated as statistically significant when the two-sided 95% CI of the SMR excludes the null value of 100.

A computet program developed by Monson[5] was used to calculate the SMRs. The program contained incorrect leukemia mortality rates for 1975 through 1979 and 1980 through 1984. We corrected the rates for 1975 through 1979 as suggested by Monson (personal communication to USDR users, May 1, 1987) and replaced the 1980 through 1984 rates with rates calculated from published US vital statistics data for 1980.[6]

Expected numbers of cell type-specific leukemia deaths were derived from 1968 US mortality data[7] for the period 1950 through 1969 and from Surveillance, Epidemiology, and End Results program mortality rates' for the period 1970 through 1984. General population mortality rates for specific leukemia cell types were not available before 1968. It is likely that cell type-specific rates increased during 1950 to 1970 as a result of more accurate diagnosis and reporting and, possibly, a true rise in incidence and mortality. If this were the *case,* the use of 1968 rates as referent rates for the period of 1950 through 1969 would overestimate the true expected numbers. Expected numbers of cell type-specific leukemia deaths were not estimated for the period 1940 through 1949. There was only one leukemia death in the study group during this period.

## Results

Of the 9484 men included in the study, 7524 (79%) had been hourly at some time during their employment at the refinery, 1871 (20%) were always salaried, 47 were salaried, unknown if ever hourly, and 42 had an unknown payroll classification. Of those who were always salaried, 1109 (59%) had held PR jobs. About 97% of the men were hired before 1940, 34% in 1940 to 1949, and 39% in 1950 or later. Fiftysne percent had worked at the refinery for at least 10 years as of Jan 1, 1984.

At the close of follow-up, 6265 (66%) men were assumed living, 2874 (30%) had died, and 345 (4%) were of unknown vital status. The total number of person-years of follow-up was 267,540, with an average length of follow-up of about 28 years. Death certificates were located for 2,733 (95%) of the men who had died. The 141 decedents for whom a death certificate was not available were included in the SMR for all causes combined (see below). However, cause-specific observed numbers of deaths and the corresponding SMRs were not adjusted to include a percentage of deaths from unknown causes. Therefore, cause-specific SMRs are underestimated by an average of 5%.

The SMR for all causes combined was 77, reflecting approximately a 20% deficit in overall mortality for the refinery workers compared with US white men (Table 1). Observed numbers of deaths for most major disease categories were fewer than expected, and most of these deficits were statistically significant.

Table 2 displays data for specific cancers. The observed number was approximately equal to or was less than the expected number for all sites except leukemia (44/29.6). The SMR for leukemia was 149 (95% CI = 108 to 200). There were statistically significant deficits of deaths from buccal cavity and pharynx cancer (6/23.5, SMR = 26, 95% CI = 9 to 56) and from lung cancer (210/249.3, SMR = 84, 95% CI = 73 to 96).

Men with long duration of employment and those with long follow-up also had statistically significant deficits of deaths for most major disease categories. Employees who had worked at the refinery for at least 10 years had an SMR of 75 (95% CI = 71 to 78) for all causes and an SMR of 82 (95% CI = 75 to 91) for all cancer. Men observed for at least 20 years since starting work had SMRs of 80 (95% CI = 77 to 84) and 87 (95% CI = 80 to 95) for all causes and all cancer, respectively.

Table 3 displays results for selected causes of death separately for hourly and salaried workers. These two groups had generally similar mortality patterns. However, the relative excess of leukemia was higher among salaried (9/3.7, SMR = 242, 95% CI = 110 to 459) than among hourly workers (35/25.7, SMR = 136, 95% CI = 95 to 190). A direct comparison of the leukemia mortality rates of salaried and hourly employees yielded a rate ratio of 1.9, with a 95% CI of 0.9 to 4.0. Within the subgroup of salaried employees, there were no striking differences between men in the PR and NPR jobs. The leukemia SMR was 192 (4/2.1) among men in PR jobs and 307 (5/1.6) among men in NPR jobs. In addition, hourly, but not salaried, workers had small increases in deaths from skin cancer (13/10.7, SMR = 121). Hodgkin's disease (8/6.7, SMR = 120), and other lymphatic and hematopoietic tissue cancer (19/16.4, SMR = 116).

Further examination of leukemia mortality patterns in the overall cohort indicated that the leukemia excess appeared to be largest in the 1950s (10/3.8, SMR = 263, 95% CI = 126 to 484), although smaller excesses also occurred in the 1960s (11/6.9, SMR = 160, 95% CI = 80 to 287) and the 1970s (16/10.6, SMR = 151, 95% CI = 86 to 245). There was no excess in 1980 through 1984 (6/7.0). Only one leukemia death occurred in the 1940s (SMR = 76).

There was no clear pattern of increasing leukemia SMRs with increasing duration of employment. However, the SMR was somewhat larger among men who had worked at the refinery for at least 10 years (33/19.8, SMR = 167, 95% CI = 115 to 235) than among men employed for fewer than 10 years (11/9.8, SMR = 112, 95% CI = 56 to 200). There was no excess of leukemia within 10 years of first hire (1/2.0). The largest excess occurred during the period 10 through 39 years since starting work (35/19.1, SMR = 183, 95% CI = 127 to 254), and there was, again, no excess after 40 years since first hire had elapsed (8/8.5).

Evaluation of leukemia mortality by period of hire and period of death revealed that, among men hired before 1940, there was a 2.5-fold increase in leukemia

TABLE 1
Observed Numbers of Deaths and Standardized Mortality Ratios (SMRs) for Major Causes of Death Among Refinery Workers, 1940 to 1984

| Cause of Death | Observed | SMR | 95% CI* |
|---|---|---|---|
| All causes | 2874† | 77 | 74–80 |
| All cancer | 661 | 86 | 80–93 |
| Infective and parasitic diseases | 14 | 23 | 12–38 |
| Benign neoplasms | 8 | 78 | 34–155 |
| Diabetes mellitus | 48 | 90 | 67–120 |
| Diseases of the | | | |
| Blood | 9 | 92 | 42–176 |
| Nervous system | 14 | 42 | 23–70 |
| Circulatory system | 1441 | 74 | 70–78 |
| Respiratory system | 136 | 57 | 48-67 |
| Digestive system | 108 | 62 | 51–74 |
| Genitourinary system | 28 | 50 | 33–73 |
| Senility and ill-defined conditions | 19 | 51 | 31–79 |
| All external causes | 228 | 74 | 65–84 |
| Other known causes | 17 | 49 | 29–78 |

* CI, confidence interval of the SMR.
† Includes 141 persons for whom a death certificate was not available.

TABLE 2
Observed Numbers of Deaths and SMRs for Selected Cancers Among Refinery Workers, 1940 to 1984

| Cancer Site | Observed | SMR | 95% CI |
|---|---|---|---|
| All sites | 661 | 86 | 80–93 |
| Buccal cavity and pharynx | 6 | 26 | 9–56 |
| Esophagus | 13 | 72 | 38–123 |
| Stomach | 27 | 67 | 44–98 |
| Large intestine and rectum | 92 | 97 | 78–119 |
| Liver | 11 | 67 | 34–120 |
| Pancreas | 31 | 75 | 51–106 |
| Larynx | 5 | 44 | 14–103 |
| Lung | 210 | 84 | 73–96 |
| Skin | 15 | 118 | 66–195 |
| Prostate | 44 | 79 | 58–107 |
| Bladder | 17 | 71 | 42–114 |
| Kidney | 18 | 95 | 57–151 |
| Central nervous system | 19 | 89 | 54–139 |
| All lymphatic and hematopoietic tissue' | 90 | 126 | 101–155 |
| Lymphosarcoma | 14 | 99 | 54–166 |
| Hodgkin's disease | 9 | 114 | 52–216 |
| Leukemia | 44 | 149 | 108–200 |
| Other lymphatic and hematopoietic tissue† | 20 | 105 | 64–162 |
| Other and unknown | 63 | 89 | 67–114 |

'Three deaths attributed to myelofibrosis are included in the category of "all lymphatic and hematopoietic tissue" but not in any of the subcategories.
† Includes other lymphoma (n = 14), multiple myeloma (n = 5) and polycythemia vera (n = 1).

TABLE 3
Observed Numbers of Deaths and SMRs by Payroll Classification

| Cause of death | Hourly (n = 7524) | | | Salaried (n = 1871) | | |
|---|---|---|---|---|---|---|
| | Observed | SMR | 95% CI | Observed | SMR | 95% CI |
| All causes | 2589 | 79 | 76–82 | 263 | 59 | 52-66 |
| All cancer | 585 | 87 | 80–95 | 68 | 72 | 56–92 |
| Buccal cavity and pharynx | 5 | 24 | 8-57 | 1 | 34 | 0-191 |
| Esophagus | 13 | 83 | 44–141 | 0 | 0 | 0-167 |
| stomach | 22 | 62 | 39–94 | 4 | 94 | 25–241 |
| Large intestine and rectum | 84 | 101 | 80–125 | 8 | 74 | 32–146 |
| Liver | 10 | 69 | 33–127 | 1 | 55 | 0-304 |
| Pancreas | 26 | 72 | 47–105 | 4 | 81 | 22–207 |
| Lung | 189 | 88 | 76–101 | 19 | 59 | 36–92 |
| Skin | 13 | 121 | 64–207 | 2 | 107 | 12-386 |
| Prostate | 41 | 82 | 59–112 | 3 | 56 | 11–162 |
| Bladder | 17 | 80 | 47–128 | 0 | 0 | 0–149 |
| Kidney | 16 | 98 | 56–159 | 2 | 83 | 9–301 |
| Central nervous system | 14 | 78 | 42–130 | 4 | 128 | 35–329 |
| LHT* | 78 | 127 | 100–158 | 12 | 129 | 66–225 |
| Lymphosarcoma | 13 | 106 | 56–182 | 1 | 54 | 0-302 |
| Hodgkin's disease | 8 | 120 | 52–237 | 1 | 84 | 1–466 |
| Leukemia | 35 | 136 | 95–190 | 9 | 242 | 110–459 |
| Other LHT | 19 | 116 | 70-181 | 1 | 40 | 0-224 |
| Other and unknown cancer | 57 | 80 | 61–104 | 8 | 76 | 33–151 |
| Circulatory diseases | 1316 | 77 | 73–81 | 117 | 54 | 45-65 |
| Respiratory diseases | 129 | 61 | 51–73 | 6 | 23 | 8-50 |
| External causes | 199 | 78 | 68–90 | 26 | 51 | 33–74 |
| Other known causes | 238 | 57 | 50–65 | 29 | 48 | 32-69 |
| Unknown | 122 | | | 17 | | |

* LHT, lymphatic and hematopoietic tissue.

(17/6.8, SMR = 251.95% CI = 146 to 402) during 1940 through 1969 and no excess thereafter (7/8.1). In contrast, among men hired in 1940 or later, no excess of leukemia was present before 1970 (5/5.2), whereas a 67% excess (15/9.6, SMR = 157, 95% CI = 88 to 859) occurred after 1969.

Table 4 displays cell type-specific observed and expected numbers of leukemia deaths by decade of death. The excess of lymphocytic leukemia was highest in 1950 through 1959 (5/1.0, SMR = 505, 95% CI = 164 to 1180), declined in 1960 through 1969 (6/2.1, SMR = 282, 95% CI = 103 to 615), and was absent in 1970 through 1984 (5/4.9). There was no excess of myelocytic leukemia in 1950 through 1959 (0/1.8) or in 1960 through 1969 (2/3.0). However, in 1970 through 1984, there was a greater than twofold increase in deaths from AML (12/5.5, SMR = 219, 95% CI = 113 to 383). Monocytic leukemia was increased from 1950 through 1979 (6/1.1, SMR = 570, 95% CI = 209 to 1241), but there was no death (0.27 expected) from this disease after 1979.

Analysis of cell type–specific leukemia by period of hire also revealed different patterns for lymphocytic and myelocytic leukemia. Men hired in or after 1940 had a 1.6-fold increase in deaths from myelocytic leukemia (11/6.9), whereas there was no excess of deaths from this disease among men hired before 1940 (4/6.1). In contrast, the excesses of lymphocytic and monocytic leukemias were not related to period of hire (lymphocytic leukemia among men hired before 1940, 9/4.5; among men hired in or after 1940, 7/3.6) (monocytic leukemia in men hired before 1940, 4/0.67; among men hired in or after 1940, 2/0.65).

TABLE 4
*observed* Number of Leukemia Deaths and SMRs* According to Decade of Death and Cell Type

| Decade | Cell Type | Observed | SMR |
|---|---|---|---|
| 1950–1959 | All lymphocytic | 5 | 505 |
| | All myelocytic | 0 | (1.8)† |
| | Monocytic | 1 | 435 |
| | Other and unspecified | 4 | 531 |
| 1960–1969 | All lymphocytic | 6 | 282 |
| | All myelocytic | 2 | 67 |
| | Monocytic | 3 | 731 |
| | Other and unspecified | 0 | (1.4) |
| 1970–1984 | Lymphocytic | 5 | 102 |
| | Acute | 1 | 130 |
| | Chronic | 4 | 119 |
| | Other | 0 | (0.76) |
| | Myelocytic | 13 | 158 |
| | Acute | 12 | 219 |
| | Chronic | 1 | 44 |
| | Other | 0 | (0.48) |
| | Monocytic | 2 | 292 |
| | Other and unspecified | 2 | 55 |

* Expected numbers for computing SMRs were estimated from US Vital Statistics, 1968[7] for deaths in 1950 through 1969 and from other data[8] for deaths in 1970 through 1984. The 1968 data do not distinguish between acute and chronic forms of lymphocytic and myelocytic leukemia.

† The expected number is provided when the observed number is zero.

Six men with leukemia mentioned on the death certificate but not coded as the underlying cause of death were not included in any of the above analyses. Three of these men were hired before 1940; two of them had lymphocytic leukemia, and one had subleukemic leukemia following myelofibrosis. The other three were hired

after 1940; two of them had unspecified leukemia and one had AML following chronic myelofibrosis.

## Discussion

The 9484 workers included in this study had an average of 28 years of follow-up during the 45-year period of 1940 to 1985. Their mortality rates for all causes combined and for most major cause of death categories were lower than those of the general US population. The overall favorable mortality experience persisted among long-term employees, and it was still present after 20 years of follow-up. These results are consistent with most previous studies of petroleum workers.[9-19] General factors that may be responsible for the apparent health advantage of these workers include selection of relatively healthy workers for employment in the industry and maintenance of their healthier status through benefits deriving from the economic advantages of employment.[20] Moreover, these findings point to the absence of occupational hazards within the industry that might have a pervasive, negative impact on employees' health.

The other noteworthy results of this study pertain to patterns of mortality from various cancers. First, there were no excesses of certain cancers found to be increased in other groups of refinery workers, including cancer of the brain, lung, stomach, pancreas, bladder, and kidney?' Among hourly employees, however, there were small, statistically nonsignificant increases in deaths from skin cancer, Hodgkin's disease, and other lymphatic and hematopoietic tissue cancer. Studies of other groups of refinery workers have reported inconsistent results for each of these diseases.

Second, there was a statistically significant 50% excess of leukemia. Only three[11,12,"] of nine[",] investigations of other groups of refinery workers have reported leukemia excesses of 10% or greater. Morgan and Wong[13] found a leukemia SMR of 173 (95%CI = 109 to 260), whereas the other two studies reported statistically nonsignificant leukemia excesses of less than 20%.

The overall leukemia excess found in the present study may be due to exposures at the refinery, to unidentified nonoccupational exposures, or to exposures at work sites other than the refinery. Chance is another possible, although unlikely, explanation of the observed leukemia patterns. Several observations argue to some extent against the hypothesis that the excess is due to refinery exposures. Salaried workers had a larger leukemia excess than did hourly workers, although the latter group probably experienced the higher exposures to chemicals at the refinery, and there was little difference in the magnitude of the leukemia excess between salaried workers in PR and NPR jobs. Also, there was no consistent increase in the leukemia SMR with duration of employment. However, these results do not detract greatly from a causal interpretation of the observed association because payroll classification and overall duration of employment may not be strongly correlated with leukemogenic exposures, if any, at the refinery.

Evaluation of leukemia mortality by cell type revealed excesses of lymphocytic, myelocytic and monocytic leukemia, some of which were dependent on period of death and period of hire. Specifically, there was a marked shift from an excess of lymphocytic leukemia among deaths occurring before 1970 to an excess of AML in 1970 through 1984. Furthermore, the myelocytic leukemia excess was restricted to men hired in 1940 or later and dying in or after 1970, whereas lymphocytic and monocytic leukemia was increased among men hired both before 1940 and in or after 1940.

Reasons for these patterns are not clear. Diagnostic techniques for cell type–specific leukemia have improved during the past few decades, and misclassification between myelocytic and lymphocytic leukemias in 1950 through 1969 may explain some of the change over time in cell type distribution.

Benzene, which is present along with other aromatic hydrocarbons in oil refineries, is considered a cause of AML[3] but not of leukemia of other cell types. Studies of rubber workers exposed to benzene, toluene, and other organic solvents have suggested that these agents are associated with chronic lymphocytic leukemia.[22,23] However, there is no firm evidence relating specific chemical agents to leukemia cell types other than that relating benzene to AML.

Manufacturing processes at the refinery have changed over time, leading to an increase in the number of units that produce or use benzene and in the percentage of benzene in refinery streams. The concentration of benzene in refinery streams was not more than 5% until 1941, when toluene units were built with one stream of 5% to 10% benzene. Benzene was also supplied by tank cars for the cumene plant (operating from 1943 to 1945) and the dodecyl benzene unit (1950 to 1954), and a coke oven product containing 65% to 88% benzene was delivered to the refinery from 1966 to early 1983. Benzene extraction units and catalytic reforming units, in operation since 1960, have benzene streams of 5% to 100%. However, it is important to note that the increased amounts and concentrations of benzene at the refinery were accompanied by enhanced efforts to control exposure. Thus, the percentage of benzene in refinery streams may not have been correlated directly with actual exposure.

Assuming that the leukemia mortality patterns by cell type, period of hire, and period of death are real and not due to disease misclassification, they have several implications:

(1) The restriction of the myelocytic leukemia excess to men hired in or after 1940 may be related to changes in exposures at the refinery in the 1940s or later. One possible explanation is an increased exposure to benzene resulting from the process changes that occurred at the refinery after 1940. However, this explanation is speculative because the changes may not have resulted in a concomitant increase in workers' benzene exposure levels and because other exposures, possibly relevant to leukemia, may have been introduced during this period. Also, the present study did not include a direct evaluation of the relation between leukemia and benzene or

other chemical exposures, and an earlier case-control study of leukemia at the refinery found no association with benzene.[2]

(2) The fact that an excess of lymphocytic leukemia was found among men hired before 1940 suggests that benzene was not entirely responsible for the overall excess of this cell type, because there was no corresponding increase in myelocytic leukemia among men hired before 1940.

(3) Finally, the lymphocytic leukemia excess diminished in 1970 through 1984. It is possible that this trend is real and reflects a reduction in some unknown leukemogenic exposure related to this cell type. In addition, the AML excess was lower in 1980 through 1984 (3/8.1, SMR = 140) than in 1970 through 1979 (9/3.3, SMR = 271), and there have been no deaths from monocytic leukemia in the 1980s. However, the expected numbers of cell type–specific leukemia deaths in 1980 through 1984 were rather small, and future observation of leukemia mortality will be necessary to evaluate the apparent reduction in the leukemia excesses in this group of workers.


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