A Historical **Prospective** Mortality Study **of** Workers in Copper and Zinc **Refineries**

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*Earlier health studies of workers in electrolytic refinery operations have raised concern that workers may experience excess morbidity and premature death as a result of hmardous occupational exposures. This study was designed to determine if the refinery operation is associated with any excess mortality patterns. A cohort of 4,802 male workers exposed for at least one year during 1946-1975 was assembled from nine U.S. zinc and copper refinerles. Vital status was ascertained for 4,241 (88%) of the **cohort.** Death certificates were obtained for 84% (3551423) of **the** deceased. Overall standard mortality ratios **(SMRs)** were calculated to be 92 for the cohort, 97 for the subgroup of copper refinery workers, and 83 for the subgroup of zinc refinery workers. Significantly high cause-specific **SMRs** were as follows: (1) cerebrovascular disease (CBVD) for the cohort; (2) all cancers, cancer of the digestive tract, and CBVD for the copper subgroup; (3) all cancers, cancer of the respiratory tract, and CBVD for **one** plant that demonstrated a significantly high overall SMR (133). The significant excess of cancer deaths among the study cohort is largely due to the plant that exhibited the significantly high overall mortality rate, but lack of smoking data qualifies this finding. The significant excess of CBVD seems to be consistent across plants and further research seems warranted to verify the finding.*

A number of studies have been published on the health hazards of occupational exposure within the copper and zinc smelting industry. Employment in this industry has been statistically associated with increased mortality from cancer of the respiratory tract, including lung cancer,[1-3] and cardiovascular **disease,**[1,3] and is possibly associated with cirrhosis of the liver, leukemia and myeloma.[3] These studies support the view that occupational exposure to arsenic in the smelter industry is particularly hazardous. A significant excess of deaths due to cancer of the respiratory tract was also noted in a group of chemical workers exposed to arsenic associated with insecticide production.[4] Furthermore, an excess of cancer of the lymphatic and hematopoietic tissues, excluding leukemia, was noted, although the numbers involved in the calculations were small. Excess lung cancer mortality has been **observed** in counties with copper, lead, or zinc smelting and refining industries, thus leading to speculation that arsenical air pollution may be hazardous to individuals living in the vicinity of these smelters.[6] However, this observation and speculations therefrom were subsequently challenged,[7] leading to an investigation[8] that yielded no association between lung cancer mortality and residence near a Utah copper smelter.

The electrolytic refining operations of major corporations have not been studied as extensively as their smelting operations in terms of the health consequences of potential occupational exposures. Surveys of electrolytic copper and zinc refining tank houses have indicated that workers in these settings may be exposed to arsenic, acid mist, and various metals such as antimony, but such occupational exposures have appeared to be minimal as a rule. Epidemiologic evidence to date concerning tank house workers has resulted from their use as a comparison group in retrospective studies of copper smelter employees, as will be discussed.

In 1977, Rencher et al[9] reported the results of a retrospective epidemiologic study of mortality that involved comparisons of copper smelting, mine, concentrator and other (control) operations of a large copper corporation. The average age at death for the four employment categories was estimated to be 63.9, 62.2, 64.9 and 59.0 years for the smelter, mine, concentrator and control groups, respectively. Proportionate analyses of cause of death revealed a higher proportion of deaths due to cancer of the respiratory tract in the smelter group compared with the other three groups and with all residents of the state in which the corporation was located; however, the control

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group, which consisted of employees in the electrolytic refinery, research center and conipany offices, demonstrated a higher proportion Of deaths for cancers other than of the respiratory tract compared with the other three groups and with state residents. Smoking information was obtained for all deceased smelter employees and for random samples of mine and concentrator decedents, but not for the control group.

A second epidemiologic study by Milby and Hine[10] was conducted on essentially the same group of employees as the study by Rencher et al,[9] but electrolytic refinery workers were examined separately and compared with employees in concentrator, mine, smelter, and reduction plants. Study results included an estimated average age at death for the refinery workers of 53.4 years, in contrast with estimates ranging from **57.4** to **70** years for other study groups.

More recently, Rencher et al[11] described the results of a retrospective epidemiologic study of morbidity as a follow-up to their earlier report. Group comparisons were made involving employees at the copper smelter, mine, concentrator and refinery. The refinery subgroup demonstrated the highest morbidity levels, both within the respiratory disease classification and *on* an overall basis. Neither of these studies included any smoking information.

Smelters and refineries represent distinct but related occupational environments, as discussed by Dungey.[12] Copper smelting is almost entirely a pyrometallurgical process in which intense heat is used to extract copper from a complex mixture of other substances in the concentrate. The smelting process produces a copper sulfide matte that is separated from slag and then oxidized in a converter to produce blister copper. Blister copper is generally fired in a refining furnace to increase its purity and then transferred to a refinery as **98%** to **99%** pure copper anodes, which are further purified through an electrolytic refining process. During electrolysis, copper travels from anodes to pure copper cathodes through an aqueous solution of copper sulfate and sulfuric acid, with impurities dropping to the bottom of tanks.

Vast amounts of particulate matter and sulfur dioxide are emitted from smelting furnaces and converters. These emissions are passed through various pollutioncontrol devices prior to venting of the residual gases to a stack. Employee exposures may be associated with fugitive emissions of these pollutants. In the refinery it is believed that minimal ernployee exposures to dust or gases occur; noise caused by slapping sheets and stacking cathodes is considered the only significant industrial hygiene problem. Since to our knowledge refinery workers have not previously been treated as a primary study group, the implications of any health problems that may occur in this occupational setting are largely unknown.

In March, **1977,** arrangements were completed for a historical prospective mortality study of nonferrous metal workers involved in the electrolytic refining of copper and zinc at nine separate plants; the results of that study are the subject of this report. A tenth plant originally intended for inclusion in the study was excluded due to inadequate reporting. The purpose of the study was to determine if employment in the zinc or copper refinery operations was associated with any health problems that might be detected by comparing the mortality experience of a large, geographically dispersed cohort of refinery workers with that of a standard population.

A cohort of **4,802** men who had been employed in the nine participating copper/zinc refineries between **1946** and **1975** was followed up to determine if they were alive at the end of **1975.** Overall, exposure-specific, plant-specific, and cause-specific standardized mortality ratios **(SMRs)** were constructed based on corresponding age-specific rates for the U.S. male population in **1970.**[13]

Methods

Prior to the start of this investigation a study was undertaken in **1976** to determine the feasibility of a historical prospective mortality study. As part of this effort, walk-through surveys were conducted at two representative facilities to evaluate current and historical exposures in both electrolytic copper refining and electrolytic zinc refining. From these surveys it appeared that zinc and copper tank houses represented different working environments with respect to potential exposure to acid mist and other potentially harmful substances such as arsenic. Therefore, the analysis of separate mortality experience for zinc tank house workers and copper tank house workers was planned as part of the study design.

Observation at each study site revealed that there was little or no meaningful distinction between the exposures entailed by the different job categories. The various jobs conducted within the tank houses involved considerable mobility about the building so that average exposures, certainly by the respiratory route, to acidic aerorols appeared to be similar for all tank house workers. Therefore, it was not planned to differentiate between different job descriptions within the tank house, but merely to ascertain total duration of employment in the tank house for each individual.

Female employees were not included in this study because they were insufficient in number to allow statistically valid analyses. A worker was included in the study cohort if he was found to have been **(1)** employed in the participating refinery as a tank house worker as of Jan. **1, 1946,** and worked for at least one year in the electrolytic department by Dec. **31, 1975;** or **(2)** hired between Jan. 1, **1946,** and Dec. **31, 1974,** and worked for at least one year in the electrolytic department.

A researcher visited each plant and microfilmed appropriate records of all past and current employees who worked in tank houses between Jan. **1, 1946,** and Oec. **31, 1975.** Microfilmed records were reviewed by the study staff and hard copies printed for all workers eligible for inclusion in the study cohort.

The study population was divided into "actives," who worked through the end of the study period (Dec. **31, 1975),** and "inactives," who terminated before the end of the study period and required follow-up. Vital status of the inactives was determined through use of death notifications filed at the employment locations together with submission of employee names and associated social security numbers to the Social Security Administration (SSA) for its review of earnings reports and death benefit applications. Copies of death certificates were obtained for members of the inactive known dead, both from the companies participat-

Plant Code	Total No.(%)	Zinc No.(%)	Copper No.(%)	Both No.(%)	Unknown No.(%)
1	856(100)	291 (34)	291 (34)	269(31)	5(1)
2	687(100)	687(100)	0 (0)	0 (0)	0(0)
3.10	3,259(100)	0 (0)	3,259(100)	0 (0)	0(0)
Total	4,802(100)	978 (20)	3,550 (74)	269 (6)	5(0)

Table 1 – Exposure by Plant

ing in the study and from bureaus of vital statistics of several jurisdictions.

For each cohort member whose vital status could not be ascertained via the SSA submission or whose death certificate could not be obtained through the agency indicated in SSA files, final attempts were made to obtain the needed information through the efforts of individual plant personnel directors. The underlying (primary) cause of death for each decedent was coded by a trained nosologist according to the International Classification of Diseases, Eighth Revision[14] and as recommended by the U.S. Public Health Service.[15]

To compute SMRs for the analysis of the cohort's mortality experience, expected numbers of deaths were calculated by (1) grouping the person-years of observation for the entire cohort and subsets thereof by five-year intervals of age at risk, (2) multiplying the person-years in each interval by the 1970 U.S. death rate for all males in that age group, and (3) summing the resultant products. A two-tailed statistical test was applied to each ratio of observed to expected deaths, assuming a Poisson distribution for the observed numbers of deaths. The Bailar-Ederer test for the ratio of a Poisson variable to its expectation was used to test departure of the ratio from unity[16]; all testing was performed at the 5% level of significance, Average age at death was also computed to provide a comparison with other estimates reported in the literature.

Results

Description of Study Population – The distribution of the study population's occupational exposure (copper, zinc, combined) by plant is given in Table 1. A majority of the men in the study were exposed to copper only (74% [3,550/4,802)) and large subgroups of these men were found in all plants except plant 2. Of the 978 *(20%)* men exposed only to zinc, all were clustered in plants 1 and 2, which reported 291 and 687 individuals, respectively.

Table 2 lists selected characteristics of the entire study cohort by plant. These figures indicate minimal variance across plants with respect to average age at hire of the study population. Indices reflecting year of hire also show minimal variance, with the exception of plant 7. For this plant, the average year hired was nine years above the grand mean, and virtually no employees were hired before 1956. With the exception of workers at plants 3, 7 and 10, the men in this cohort were almost exclusively white. The apparently small number of nonwhite workers, coupled with differential reporting of race across plant records (race unknown for 22.5% of the entire cohort), prohibited the application of any reliable race-specific analyses.

Follow-up of Study Population – Table 3 shows the vital status of the study population by plant as of Dec. 31, 1975. Of the 4,802 workers in the study, complete follow-up was achieved for 4,241 (88%) individuals. The unknown rate by plant varied between 5% (plant 6) and 17% (plant 10). Of the 423 (9%) men known to have died, death certificates were obtained for 355 (84%). Eight of these certificates, however, had either missing or illegible cause of death information; men in this subgroup were necessarily eliminated from analyses of specific causes of death. The plant-specific success rates for obtaining death Certificates for study decedents varied between 63% (plant 7) and 97% (plant 8).

Table 4 gives the vital status of the population by exposure as of Dec. 31, 1975. The unknown rate by exposure was 12% for the copper- and combined-exposure groups and 11% for the zinc-exposure group.

Further details concerning the study's success vis-à-vis ascertainment of vital status and procurement of death certificates are seen in the Fig. For 38 decedents whose certificates were in the custody of the New York City Health Department (and who are included in the count of 355 obtained certificates), causes of death were abstracted by that agency, forwarded to the study team, and coded by the study nosologist. Although causes of death were not associated with specific individuals for reasons of confidentiality, the identities of individuals for whom certificates could be located were revealed, and all such persons were found to be copper refinery workers employed at plant 10. Thus, these 38 deaths were included iri all exposure-specific, plant-specific, age-specific and cause-specific SMR analyses.

Table 2 – Age, Race, and Him Data Characteristics by Plant

Characteristics	Plant* 1 (Zinc)	1 (Copper)	1 (Both)	2	3	4	6	7	8	9	10	All Zinc	All Copper	All Plants
No. in Cohort	291	291	269	687	504	474	303	357	407	650	564	978	3,550	4,802
Average age at hire, yr	24	26	24	29	29	29	24	28	27	27	31	26	28	27
Average year hired, yr	1956	1957	1955	1959	1954	1953	1956	1965	1955	1957	1954	1958	1956	1956
%hired before 1956	40	43	46	43	59	53	38	0	7	43	47	42	46	45
%white race	98	98	99	100	68	97	97	43	100	92	48	99	79	84

- individuals at plant 1 worked with either Zn or Cu or both; individuals at plant 2 worked with Zn; and individuals at plants 3 through 10 worked with Cu; five individuals at plant 1 with unknown exposure status are included only in summary figures

Table 3 – Follow-up Status of 4,802 Copper and Zinc Refinery Worken by Plant

Plant Code	Total No.(%)	Alive No.(%)	Oead No.(%)	Unknown No.(%)	Death Certificate Received No.(%)	Death Certificate Not Received No.(%)
1	856(100)	673(79)	58 (7)	125(15)	52(90)	6(10)
2	687(100)	575(84)	49 (7)	63 (9)	43(88)	6(12)
3	504(100)	374(74)	64(13)	66(13)	52(81)	12(19)
4	474(100)	365(77)	82(17)	27 (6)	72(88)	10(12)
6	303(100)	266(88)	21 (7)	16 (5)	16(76)	5(24)
1	357(100)	312(87)	8 (2)	37(10)	5(63)	3(37)
8	407(100)	330(81)	35 (9)	42(10)	34(97)	1 (3)
9	650(100)	532(82)	30 (5)	88(14)	22(73)	8(27)
10	564(100)	391(69)	76(13)	97(17)	59(78)	17(22)
Total	4,802(100)	3,818(80)	423 (9)	561(12)	355(84)	68(16)

Exposure-Specific, Plant-Specific, and Age-Specific Analyses – It was previously noted that comparisons between zinc and copper workers were planned as part of the study design. Comparisons by plant and by age group were also performed. Such internal comparisons have been advocated in the occupational health literature,[17,18] particularly when a general reference population is used for SMR calculations. Decedent characteristics used for these comparisons are presented by expcsure status and plant in Table 5. The characteristics for each group of workers are number of decedents, average age at death for the decedents, overall SMR and SMRs for five 10-year age groups within which all but one study death occurred.

The SMR for the entire cohort is 92. The highest SMR by exposure group is an SMR of *97* for copper workers; SMRs are equal to 83 for the zinc workers and 53 for the workers exposed to both substances. Average age at death is highest for the workers with combined zinc/copper exposure. Although the low SMR for combined exposure is statistically significant, this subgroup consists of only **269** uorkers who were all employed at plant 1.

The average age at death across all plants for the deceased group was *58* years. The SMR of 133 for plant 4 is significantly higher than unity and the SMR of 54 for plant 9 is significantly lower than unity. The respective average ages at death (59 and 60) for these two plants, however, are consistent with the average age at death across all plants. The markedly low average age at death for plant 7 (34 years) seems to be associated with the relatively late average year of hire (1965) and low average age at hire (28) for that plant (Table 2) and serves to illustrate the incomparability of age at death statistics across studies unless factors such as average age at hire, average year hired, and length of follow-up are also considered.

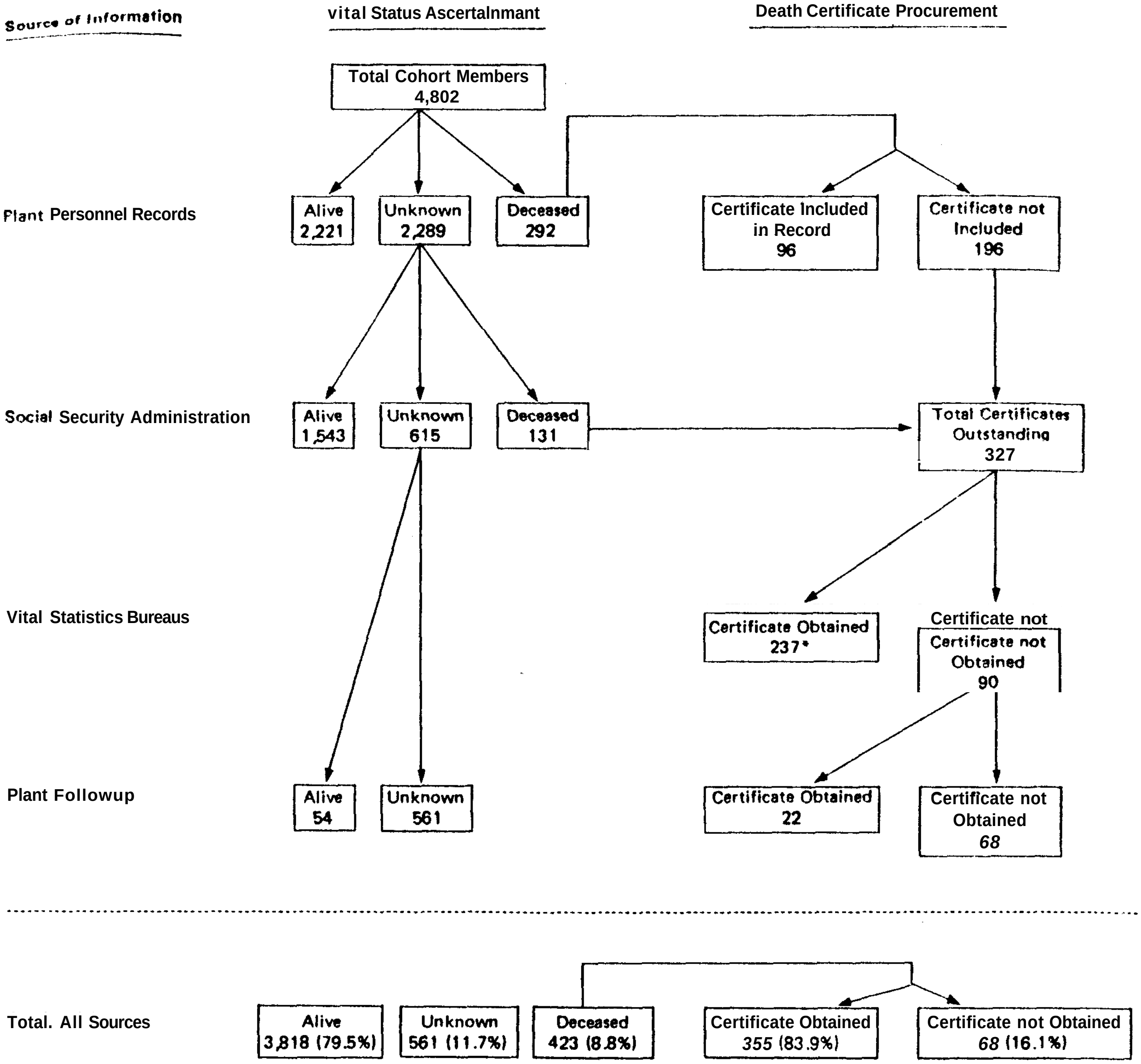
The SMRs by age group in Table **5** are given to address the phenomenon known as the "healthy worker effect," which has been discussed in some detail by McMichael.[19] He has noted that such an effect, which presumably stems from an initial better-than-average health status of persons entering most work environments, tends to disappear and perhaps reverse with increasing age. For the present exercise, observed and expected deaths in pairs of adjacent five-year age intervals were combined to lend some stability to the resultant SMRs. Despite aggregation, some SMRs are based on fewer than 100 person-years at risk and there are no person-years at risk at plant 7 for the oldest age group (65 through 74 years).

While the age-specific SMRs for the total cohort and for the copper and zinc subgroups are consistent with the healthy worker effect, this phenomenon clearly does not operate uniformly across individual plants. In particular, observed deaths exceed those expected for the four youngest age groups at plant 4 and for the three middle age groups at plants 8 and 10. Excess deaths are also apparent among the youngest age group at plants 6 and 7 and among the youngest zinc workers at plant 1.

Some additional decedent characteristics not included in Table *5* are noteworthy. The average year of hire for the

Table 4 – Followup Status of 4,802 Copper and Zinc Refinery Worken by Exposure

Exposure	Total No.(%)	Alive No.(%)	Dead No.(%)	Unknown No.(%)	Death Certificate Received No.(%)	Death Certificate Not Received No.(%)
Zinc	978(100)	793 (81)	73(7)	112(11)	62(85)	11(15)
Copper	3,550(100)	2,797 (79)	355(9)	418(12)	279(83)	56(17)
Both	269(100)	223 (83)	15(6)	31(12)	14(93)	1 (7)
Unknown	5(100)	5(100)	0(0)	0 (0)	0 (0)	0 (0)
Total	4,802(100)	3,818 (80)	423(9)	561(12)	355(84)	68(16)



* Includes 38 deceased for whom New York City Health Department did not release death certificate but abstracted cause of death information

Flow of record ascertainment in the study.

deceased was **1942,** with **89%** having a hire date before 1956. The difference between average age at death and at hire was 25 years, indicating that potential latency effects associated with zinc/copper can probably be discerned from the collective cohort experience. The interval between hire date and date of death was **20** years or more for 67% of the deceased group and ten years or more for an additional 21% of the group. Most researchers studying latency periods have chosen **20** years or more duration since first exposure as a latency definition.[17]

Cause-Specific Analyses – Table **6** presents cause-specific **SMRs** for major causes of death among the **4,802** male refinery workers, based on 347 decedents for whom the underlying cause of death could be assigned by the study nosologist. The observed numbers of deaths by cause generally are not significantly different from expectation, with the exception of deaths from major cardiovascular diseases **(SMR, 84),** particularly heart disease (SMR, 78), from cirrhosis of the liver **(SMR, 24),** and from accidents **(SMR, 53)**, suicide **(SMR,** 41) and homicide **(SMR, 44),** all **of** which are significantly lower than expected.

For the malignant neoplasms, **SMRs** are over 100 for cancer of the digestive system (105), cancer of the genitals (159), cancer of the urinary tract (103), and "other" lymphomas and neoplasms (104). None of these ratios, however, are significantly greater than 100. Also, although the SMR for major cardiovascular diseases (84) is significantlv lower than 100. it is interesting to note the

Table 5 – Decedent Characteristics by Plant and Exposure

Characteristics	Plant* 1 (Zinc)	1 (Copper)	1 (Both)	2	3	4	6	7	8	9	10	All Zinc	All Copper	All Plants
No. of Decedents	24	19	15	49	64	82	21	8	35	30	76	73	335	423
Average age at death, yr	59	61	67	58	60	59	52	34	48	60	61	58	57	58
SMR	69	73	53†	93	109	133†	74	88	104	54†	105	83	97	92
Age specific SMRs, age group														
25-34	118	44	00	70	71	115	129	183	76	33	27	81	79	74
35-44	92	00	00	52	96	110	93	61	125	31	148	62	90	79
45-54	28	85	27	116	110	209	58	52	119	49	111	88	110	101
55-64	71	193	111	141	93	132	47	00$	137	45	110	102	101	103
65-74	161	36$	193‡	162	217	92	140‡	...	00$	301‡	137	161	140	146

- * Individuals at plant 1 worked with either zinc or copper or both; individuals at plant 2 worked with zinc, and individuals at plants 3 through 10 worked with copper
- † Statistically Significant at the .05 level
- ‡ Based on fewer than 100 person-years at risk

excess (124) for cerebrovascular disease (CBVD). This excess, however, fails to achieve the 5% level of significance. For a supplemental analysis, deaths with unknown causes were allocated to specific disease categories in proportion to the distribution of deaths with known causes. (Of the 423 deaths among the cohort, 68 had no available death certificates and eight had certificates with missing/illegible cause of death.) Following this adjustment, the SMRs for cirrhosis of the liver (29) and accidents (65) remain significantly lower than unity while the SMRs for hypertensive heart disease (339) and CBVD (151), particularly cerebral thrombosis (204), become significantly higher than unity. However, the SMRs for cirrhosis of the liver and hypertensive heart disease are based on fewer than five observed deaths each.

Since 74% of the study cohort were exposed only to copper and were employed in eight of the nine plants, it was considered important to present SMRs for selected causes of death for the 335 decedents in this major subgroup (Table 7). The only significant SMR prior to allocation of 64 deaths with unknown causes is for ischemic heart disease (78), with the SMR for CBVD (148) falling just short of its critical value (149). However, after allocation of deaths with unknown causes, the SMR for ischemic heart disease (97) is no longer significant but SMRs for all cancers (128), the subgroup of cancers of the digestive tract (157), and CBVD (183) are significantly high.

Since the overall SMR for plant 4 was found to be significantly high, an examination of mortality from selected causes was also performed for the 82 deaths associated with that plant (Table 7). Although no cause-specific SMRs based on the 72 deaths with cause-of-death information are significant, several causes have elevated SMRs, including all cancers (157), cancers of the digestive tract (199), cancers of the respiratory tract (191), major cardiovascular disease (122), and CBVD (221). On allocating the ten deaths with unknown causes in the manner described previously, the SMRs for all cancers (179), cancers of the respiratory tract (218), and CBVD (252) attain significance.

Since the overall SMR for plant 4 was noted to be significantly high, it is natural to question whether this particular plant accounts for the excess cause-specific mortality previously detected for the copper refinery cohort following the allocation of deaths with unknown causes. This question can be addressed by comparing the SMRs in parentheses for all copper refinery workers, plant 4 workers, and other plant workers in Table 7. From this evidence, it is apparent that plant 4 accounts for the majority and statistical significance of excess deaths due to cancer experienced by the copper cohort, since the SMR of 110 for malignant neoplasms among workers at other plants is not significant. Even though the SMR for cancers of the respiratory system among all copper workers is elevated (114) hut not statistically significant, plant 4 does account for all excess deaths in this category. The significant excess of deaths among all copper workers from cancers of the digestive system is not significant in either subcategory, but is elevated in each. The only disease category for which the significant excess among all workers persists within both subcategories is CBVD.

Discussion

This investigation represents a historical prospective mortality study of 4,802 men who had been employed in one of nine participating copper and zinc refineries. These refineries, corresponding to seven copper plants, one zinc plant, and one copper/zinc plant, are located in various geographic areas throughout the United States and represent five of the major copper or zinc corporations. To our knowledge, this multicenter study is one of the first of its kind since it permitted internal comparisons of the entire cohort based on type of exposure and individual plant experiences, in addition to a "pooled" cause-specific mortality analysis.

The cause-specific SMRs relating to the entire cohort showed no rates significantly higher than expectation, although the rates were significantly low for major cardiovascular diseases, cirrhosis of the liver, and accidents, suicide and homicide. The SMRs for some cancer sites were somewhat elevated, but, again, none were significantly

Table 6 – Cause-Specific SMRs for All Refinery Workers				
ICD No.*	Disease Category	No. of Observed Deaths	No. of Expected Deaths	SMR†
000.999	All causes	423	461.905	92 ...
090·097	Syphilis	1	0.103	969 (1,184)
140.209	Malignant neoplasms	75	81.058	93 (113)
150·159	Cancer of the digestive system	22	20.883	105 (128)
160-163	Cancer of the respiratory system	25	28.605	87 (107)
180·187	Cancer of genitals	7	4.411	159 (193)
188·189	Cancer of the urinary tract	4	3.900	103 (125)
170·173, 190-199	Other malignant neoplasms	10	10.982	91 (111)
204·207	Leukemia	1	3.461	29 (35)
200·203, 208, 209	Other lymphomas, neoplasms	6	5.788	104 (126)
210·239	Benign neoplasms	1	1.292	77 (94)
250	Diabetes	6	6.161	89 (108)
390·448	Major cardiovascular diseases	167	199.162	84‡ (102)
390-398,402,404,410-429	Heart disease	127	163.359	78‡ (95)
402	Hypertensive heart disease	4	1.437	278 (339‡)
410-413	Ischemic heart disease	114	146.834	78 (95)
410	Acute myocardial infarction	66	99.510	66 (81)
411	Other acute ischemic heart disease	3	1.396	215 (262)
412	Chronic ischemic heart disease	45	45.869	98 (120)
430-438	Cerebrovascular disease	33	26.591	124 (151‡)
431	Cerebral hemorrhage	7	7.717	91 (111)
433	Cerebral thrombosis	9	5.385	167 (204‡)
430, 432, 435·438	Other cerebral diseases	17	13.364	127 (155)
440	Arteriosclerosis	1	1.993	50 (61)
441·448	Other diseases of the arteries	6	5.281	114 (138)
470·474, 480·486	Influenza and pneumonia	5	11.349	44 (54)
490-493	Bronchitis, emphysema, asthma	5	8.216	61 (74)
571	Cirrhosis of the liver	4	16.951	24‡ (29‡)
580·584	Nephritis and nephrosis	3	2.581	116 (142)
600	Hyperplasia of prostate	1	0.323	301 (377)
800·949	Accidents	29	54.514	53‡ (65‡)
950.959	Suicide	6	14.716	41‡ (50)
960·978	Homicide	6	13.591	44‡ (54)
	All other known causes	38	51.288	74 (90)
	Unknown causes	76	...	...

* ICD indicates International Classification of Diseases, Eighth Revision
† The SMRs in parentheses were calculated following allocation of 76 deaths with unknown causes
‡ Statistically significant at the .05 level

higher than expected. Adjustments were also made to the SMRs by proportionally allocating deaths with unknown causes. Following this adjustment, only the SMRs for CBVD and hypertensive heart disease became significantly high and only the SMRs for cirrhosis of the liver and accidents remained significantly low, with hypertensive heart disease and cirrhosis of the liver each accounting for fewer than five observed deaths. Since a majority of the cohort was exposed only to copper, we also determined cause-specific SMRs for this subgroup. A significantly low SMR was noted for ischemic heart disease prior to allocation of diseases with unknown causes; however, following adjustment for these unknowns, a significant excess of deaths was detected for all cancers, cancers of the digestive tract and CBVD. Finally, since the overall SMR for plant 4 was significantly high, we also investigated the cause-specific SMRs relating to this particular plant, After allocation of unknown causes, significantly high SMRs were noted for all cancers, cancers of the respiratory tract, and CBVD. It was further discerned that plant 4 accounted for the majority of excess deaths due to cancer among the copper refinery cohort, but that the significant excess of deaths due to CBVD following allocation of unknowns persisted both among workers at plant 4 and among the combined workers at other study plants.

It was not determined if the increased mortality effect from CBVD identified in this study showed any gradient with length of employment, but the deceased group did

Table 7 – No. of Observed and Expected Deaths for Selected Disease Categories Among All Copper Refinery Workers, Copper Refinery Workers at Plant 4, and Copper Refinery Workers at Other Study Plants

	All Copper Refinery Workers		Rant 4 Workers		Other Plant Workers	
Disease Category	Observed/ Expected Deaths	SMR*	Observed/ Expected Deaths	SMR*	Observed/ Expected Deaths	SMR'
Malignant neoplasms	63/61.01	130 (128†)	18/11.48	157(179†)	45149.53	91 (110)
Digestive organs and peritoneum	20115.71	127 (157†)	613.01	199(227)	14/12.70	110 (133)
Respiratory system	20/21.68	92 (114)	814.18	191(218†)	12117.50	69 (83)
Genitourinary organs	816.16	130 (161)	1/1.19	84(96)	7/4.97	111 (170)
Lymphatic and hematopoietic tissue	616.93	87 (107)	311.21	248(282)	3i5.72	52 (63)
Major cardiovascular disease	1281148.65	86 (106)	34127.82	122(139)	94/120.83	78†(94)
Ischemic heart disease	861109.92	78†(97)	22/20.32	108(123)	64/89.60	71t(86)
Cerebrovascular disease	29/19.58	148 (183†)	8/3.62	221(252†)	21/15.96	132 (159†)

• The SMRs in parentheses were calculated following proportional allocation of deaths with unknown causes; death with known/unknown causes were 335164 for all copper workers, 72/10 for plant 4 workers, and 263/54 for other plant workers

† Statistically significant at the .05 level

consist primarily of men who had been hired 20 years before the end of the study period (89% hired before 1956). Thus, the CBVD effect may be related to exposures in the refinery or to other factors not considered herein. It is interesting to note, however, that an SMR of 450 for CBVD had been noted earlier among workers at a Swedish copper smelter[3] which, when the data base was stratified to eliminate the confounding effect of arsenic exposure, still appeared as an SMR of 170 (p=.07 based on a one-tailed test) for copper exposure only. A more recent study of Swedish copper smelter workers[20] demonstrated a similar significant effect for CBVD (SMR=157; p<.01 based on a two-tailed test).

A recent review of the epidemiology of stroke by Ostfeld[21] pointed out that high blood pressure (BP) is the most important risk factor for stroke and that heart disease and diabetes are also major disease contributors to the risk of stroke. It is possible that either high BP or diabetes or both were disproportionately high in occurrence among the study cohort and accounted for the high cerebrovascular ratio for the entire cohort, for the subgroup of workers exposed to copper, and for workers in plant 4. The SMR for hypertensive heart disease in this study was significantly high for the entire cohort although the number of deaths attributed to this disease was relatively small; the issue of contributory causes of death was not examined.

Ostfeld's review did not implicate cigarette smoking as a major contributor to strokes. Thus, although cigarette smoking was not analyzed in this study, lack of data on this factor would not seem to have had a confounding influence on the apparent CBVD effect. Since blacks are known to be at greater risk of mortality from strokes than whites, the racial distribution of CBVD decedents was examined. The proportion of nonwhites among these decedents was lower than the corresponding proportion among the entire cohort, thereby ruling out the confounding effect of race on stroke mortality in this study. Finally, Ostfeld noted the difficulties in diagnosing stroke and the fact that stroke and heart disease represent competing risks for mortality. The finding of an excess of deaths due to CBVD and a shortfall of deaths due to heart disease in this study is consistent with that notion.

The finding of a significant excess of deaths due to cancer among the copper refinery cohort in this study is subject to multiple interpretations. Wagner[22] has indicated in a report on environmental conditions in smelters in the United States that arsenic-induced cancers probably exist in this industry. Though it is tempting to apply this specula-

Table 8 – Percent of U.S. Male Deaths Among Selected Ape Groups Caused by Selected Diseases"

	Diseases			
Age Group, yr	All Malignant Neoplasms	Cancers of Digestive Tract	Cancers of Respiratory Tract	Cerebrovascular Disease
40-44	14.4	3.1	5.2	4.2
45-49	17.5	4.2	6.7	4.4
50-54	20.3	5.2	8.1	4.8
55.59	22.2	5.9	9.0	54
60.64	22.6	6.3	8.7	6.6
65.69	21.6	6.2	7.8	8.2
70.74	19.7	6.2	6.2	10.2

• Source: U.S. Public Health Service, Vital Statistics of the United States, 1970[13] tion to refinery workers, most refineries in this study are not geographically proximate to smelters and, as noted earlier, potential arsenic exposures in the refinery seem to exist only at low concentration levels.

The major exception to the point made above is study plant 4, where the refinery is directly adjacent to the smelter. This plant was previously noted to account for the majority of excess deaths due to cancer in this study and, more specifically, for all excess deaths due to cancers of the respiratory system. Many of the employees at plant 4 are older workers who have bid into the refinery from the smelter after attaining sufficient seniority; a smaller proportion of workers are assigned to the less demanding work in the refinery because of a handicap, disability, or chronic health problem (Lowell D. White, Written Communication June 4, 1981). Thus, the analysis of cancer mortality at this plant is confounded by prior occupational exposures that most likely are more severe than those experienced in the refinery together with a possible reversal of healthy worker effect. At plant 8, the smelter and refinery are about a mile apart and the refinery workers similarly may have transferred from the smelter and probably represent a higher proportion of disabling or chronic conditions than in most work settings. The SMRs greater than 100 were previously noted for the four youngest age groups at plant 4 and the three middle age groups at plant 8.

Since all cancers of the respiratory tract detected among the study cohort were specifically cancers of the lung, it follows that the SMR for this anatomical site would be higher than that for cancers of the respiratory tract as a group. However, the lack of smoking data for this cohort qualifies any findings with respect to lung cancer. Sterling and Weinkam[23] have used data from the 1970 Household Interview Survey (HIS) conducted by the National Center for Health Statistics to demonstrate that smoking prevalence tends to be uniformly highest among blue collar workers. A survey[24] of workers at a Garfield, Utah, smelter yielded estimates that 69.9% of white male workers had ever smoked, a figure that does not differ appreciably from the corresponding HIS estimate of 69.2% for white males. However, the Garfield survey data further indicate that 33.6% of the smelter workers smoked a pack of cigarettes or more per day, in comparison to HIS estimates of 28%. Moreover, a survey[5] of retirees from a Tacoma, Wash. smelter estimated that 50% of those individuals were current smokers, as contrasted with HIS estimates that 23% of males aged 65 and over currently smoked. If the two surveys are indicative of smelter worker smoking habits, then these workers tend to smoke more intensively and abandon the smoking habit less frequently than U.S. males as a whole. However, the extent to which findings among smelter workers are applicable to the refinery setting cannot be discerned from available data.

Although there are precedents[25,26] in the occupational research literature for allocating deaths with unknown causes in the manner used in this study, potential biases associated with such an approach should be explored. Selected comparisons between deceased with death certificates and those without indicate that such biases should be minimal in this study. The distributions of the two groups with respect to calendar year of death were virtually identical so that possible distortions attributable to changing customs for assigning cause of death should not manifest themselves here. On the other hand, the average age at death for the deceased without certificates was more than six years lower than that for the group with certificates. If the disease categories in which excess study deaths occurred also claim an increasing proportion of deaths with increasing age, then the allocation process will have favored these diseases. Data in Table 8, presented for age groups in which nearly 90% of study deaths occurred, show this to be the case; however, the average increase in percentage of lives claimed over successive five-year age intervals is only about one percentage point for CBVD and malignant neoplasms and is a lesser amount for the cancer subcategories of interest. Thus, on the basis of these data, the process may have "overallocated" at most one death to any of the disease categories, since the total number of study deaths with unknown causes was 76. Such a minimal distortion should not have an impact on study findings.

Our use of U.S. male mortality rates as the standard in calculating SMRs is justified in the sense that the nine study plants are geographically dispersed and their collective racial distribution is similar to that among U.S. males. Though we may be open to criticism for using 1970 rates in lieu of sets of rates specific to calendar years, deaths among the study cohort tended to cluster in the ten-year period between 1966 and 1975. According to the review of Silverberg and Holleb[27] of major trends in cancer over a recent 25-year period, age-adjusted cancer death rates generally remained constant over that period although a decrease was noted for stomach cancer and an increase was noted for lung cancer. A review[28] of the leading causes of death over the period 1950-1969 indicated increases for malignant neoplasms and decreases for CBVD. In view of this evidence, our use of 1970 rates as a standard may have inflated SMRs for CBVO and cancers of the digestive tract and deflated SMRs for cancer in general and the subset of cancers of the respiratory tract. However, such biases should again be minimal since most study deaths were proximate in time to the year 1970.

The results of this study seem to shed additional light on conflicting "age at death" statistics reported from earlier studies. Rencher et al[9] reported average ages at hire and at death of 32.3 and 59.0 years from their 1977 study of refinery workers at a Utah copper plant. Our corresponding figures are 32 and 48 years for a Utah copper plant and 33 and 58 years across all study plants. While their statistics are based on deaths between 1959 and 1969 for one plant, our overall figures are based on deaths between 1946 and 1975 for nine plants. Thus, our figures have a more comprehensive base, both in terms of industry representiveness and coverage of time. Milby and Hine's[10] average age at death estimate of 53.4 for Utah refinery workers had no accompanying age at hire statistics and was based on deaths between 1950 and 1972 among those who worked for ten years or more for one company and, furthermore, had a complete work history available.

Since average-age-at-death statistics from this and prior related studies are not based on the complete follow-up experience of any cohort, they are not valid indicators of premature death and are not truly intercomparable. A suggested statistic for future comparisons is the expected age at death, as discussed by Gaffey.[29] This statistic may be

Table 9 – Mortality Rates and Probability of Death by Age for All Refinery Workers and for U.S. Males in 1970

Age Group, yr	Person-Years at Risk	1-yr Mortality Rates: Refinery Workers	1-yr Mortality Rates: 1970 U.S. Males	SMR	Probability of Death During 5-yr Interval*: Refinery Workers	Probability of Death During 5-yr Interval*: 1970 U.S. Males	Relative Risk
15-19†	669.3	...	...	...	...	...	...
20-24	5534.2	0.000181	0.002257	8	0.000905	0.011222	8
25-29	8809.9	0.001249	0.002027	62	0.006226	0.010084	62
30-34	9354.5	0.001924	0.002301	84	0.009574	0.011439	84
35-39	9278.2	0.001940	0.003142	62	0.009653	0.015587	62
40-44	8600.4	0.004418	0.004849	91	0.021848	0.023954	91
45.49	7336.2	0.006816	0.007567	90	0.033506	0.037128	90
50-54	5565.9	0.012936	0.011793	110	0.062633	0.057260	109
55-59	3156.9	0.019679	0.018572	106	0.093791	0.088679	106
60-64	2047.5	0.027350	0.027863	98	0.127812	0.130046	98
65-69	768.4	0.071577	0.041179	174	0.300847	0.186082	162
70-74	415.5	0.064982	0.058934	110	0.277408	0.255223	109
> 75†	313.1	...	...	...	...	...	...

- Equal to $1-e^{-(\text{1-year mortality rate} \times 5)}$ for a given age group

† No decedents from the cohort within these age groups

calculated by life-table methods with knowledge of the relationship between age-specific mortality rates and probabilities of death during specific age intervals, as discussed by Chiang.[30] Inputs to the calculation of expected age at death for all refinery workers and the subset of copper refinery workers in this study appear in Tables 9 and 10, respectively. Since there were no cohort decedents aged 75 or older, it was assumed that workers reaching age 75 would live to an average age of 83.3 years, based on 1970 U.S. life-table values for this age group.[13]

The expected age-at-death statistic utilizes the experience of an entire worker cohort and may be interpreted as life expectancy on entering a given work environment at a specific age. From the inputs in Tables 9 and 10, the expected age at death for workers entering at age 20 is estimated to be 69.35 years for all refinery workers and 69.15 years for the subgroup of copper refinery workers. The entire cohort has an average age at hire of *27* years and an average year of hire of 1956. By comparison, expected age at death for the U.S. white male population aged 20 years during 1949-1951 was estimated to be 69.5 years.[31] Thus, from evidence in this study, employment at the refinery does not seem to be associated with premature death. However, use of a U.S. life-table value for workers reaching age 75 tends to bias refinery workers' life expectancy toward that of the U.S. population.

Table 10 – Mortality Rates and Probability of Death by Age for Copper Refinery Workers and for U.S. Males in 1970

Age Group, yr	Person-Years at Risk	1-yr Mortality Rates: Refinery Workers	1-yr Mortality Rates: 1970 U.S. Males	SMR	Probability of Death During 5-yr Interval*: Refinery Workers	Probability of Death During 5-yr Interval*: 1970 U.S. Males	Relative Risk
15-19†	359.9	...	...	...	...	...	...
20-24	3751.9	0.000267	0.002257	12	0.001334	0.011222	12
25.29	6421.5	0.001402	0.002027	69	0.006986	0.010084	69
30.34	7063.4	0.001982	0.002301	86	0.009861	0.011439	86
35-39	7003.3	0.002285	0.003142	73	0.011360	0.015587	73
40-44	6448.8	0.004962	0.004849	102	0.024505	0.023954	102
45.49	5561.6	0.007552	0.007567	100	0.031056	0.037128	100
50-54	4210.0	0.014014	0.011793	119	0.067671	0.057260	118
55-59	2879.0	0.018757	0.018572	101	0.089522	0.088679	101
60-64	1556.7	0.028265	0.027863	101	0.131793	0.130046	101
65-69	598.2	0.066867	0.041179	162	0.284186	0.186082	153
70.74	322.4	0.065137	0.058934	111	0.271967	0.255223	109
≥ 75†	199.4	...	...	...	...	...	...

- Equal to $1-e^{-(\text{1-year mortality rate} \times 5)}$ for a given age group

† No decedents from the cohort within these age groups

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The study results are essentially negative, with most positive findings subject to qualification. The significant excess of deaths due to cancer among the study cohort following allocations of deaths with unknown causes was largely attributable to excess deaths due to cancer at one study plant. Unlike other study plants, its refinery is directly adjacent to a smelter; a number of workers at this refinery have transferred from the adjacent smelter wherein more severe occupational exposures probably occurred arid these workers as a group are believed to possess a higher proportion of disabling or chronic conditions than in most work settings. Lack of smoking data further qualifies the study results with respect to cancer and, in particular, with respect to the significant excess of cancers of the respiratory tract at the refinery cited above. A significant excess of study deaths from CBVD, however, could not be attributed to that plant alone. The findings with respect to CBVD are similar to those found in several earlier studies of smelter workers, although smelters and refineries probably do not represent similar exposure environments. A possible qualifier to the CBVD excess is the notion of competing risks, especially since the SMR for ischemic heart disease in this study was lower than unity. If the CBVD effect is a real association, it will be necessary to determine which occupational factor(s) contribute to the excess. For example, noise may be involved as a risk factor[32] based on an understanding of the refinery environment.

Potential biases associated with the allocation of deaths with unknown causes and with the use of 1970 mortality rates for SMR calculations were investigated and considered to be negligible. An exercise based on life-table methods indicated that employment in the study refineries did not appear to be associated with premature death. The study would benefit from an additional five years of follow-up information, coupled with more intensive efforts toward death certificate procurement, since any significant excesses of cause-specific mortality followed the allocation of deaths with unknown causes. The 200 or more deaths expected between 1976 and 1980 for this cohort, together with increasing years-at-risk contributions from older cohort members, would tend to stabilize the age- and cause-specific SMRs reported at this time. Further research may be warranted to substantiate the positive findings of Rencher et al[11] with respect to refinery worker morbidity patterns, but studies that do not include ancillary data on smoking behavior are not recommended.

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