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MORTALITY AMONG EMPLOYEES ENGAGED IN CHEMICAL MANUFACTURING AND RELATED ACTIVITIES

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A retrospective cohort mortality study was conducted among men employed for one or more years, between 1940 and 1969, at an operating division of a large chemical company. Vital status follow-up for the cohort of 1,919 men was determined through 1979 and identified 390 deaths. Overall mortality in the study group and in each of eight employment subgroups was less than that of the corresponding United States white male population. Additionally, standardized mortality ratios were not significantly elevated for any of the examined cause-of-death categories. Cause-specific mortality comparisons were also made among the employment subgroups and by duration of employment in the company division using an internal analysis method. There were no relationships observed for employment duration. Several significant differences ($p < 0.05$) by employment subgroup were noted; however, neither the decreases nor increases presently could be ascribed to identifiable environmental factors.

environmental exposure; mortality; occupational diseases

Evaluation of mortality is integral to the development of a comprehensive occupational health surveillance program. Deviations in mortality patterns of exposed groups from expected patterns may target areas in need of preventive intervention, provide important clues for further research, or provide information regarding the safety of specific industrial operations.

A common difficulty in conducting such research is that of determining what the expected pattern of mortality should be in the absence of specific exposures. The expedient solution to this difficulty is to base comparisons on era- and age-specific death rates derived from general population mortality tables. Such a solution has been criticized, however, because fitness for work, a selection characteristic of employee populations, is not operative in general populations. Thus, an employee group would likely experience favorable mortality relative to the corresponding community population for certain diseases and for some period after initial employment (1, 2).

An alternate approach is to develop mortality information for a total employee population and to perform internal comparisons for well-defined subsets of that population. This approach is feasible in companies with diverse operations and was so used in the present study as a supplement to the more conventional comparisons with general population mortality data.

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The specific objectives of this study were: 1) to describe the baseline mortality experience of men assigned to the Western Division of The Dow Chemical Company; 2) to examine socioeconomic status and years of employment as determinants of mortality in this industrial population; and, 3) to assess cause-specific mortality in relation to eight general employment categories using both internal company and general population comparisons.

MATERIALS AND METHODS

The study population was identified by reviewing all job history records on file at the Pittsburg/Walnut Creek, or Torrance, California locations of The Dow Chemical Company. The employee job record card contains identifying and demographic information for each employee as well as a listing of all prior job assignments. Men were entered into the study if employed at either of the respective locations on January 1, 1940, or at some time prior to December 31, 1969. Furthermore, to be eligible, an employee must have worked continuously for at least one year at either of the previous listed company locations. Women employees were excluded from the study cohort since most women have been assigned to office areas. Initial data obtained for each individual included name, Social Security number, birth date, sex, race, and excerpts of employee job histories. The job history components consisted of job titles and dates for each organizational unit in which the employee had worked one or more years and final employment status (working, retired, or left before retirement). The period of mortality follow-up was from 1940 through 1979, with vital status determination based on company records for active and retired employees, and based on Social Security Administration follow-up for terminated employees. In either case, copies of death certificates were obtained and underlying cause of death was coded by an experienced nosologist according to the revision of the International Classification of Diseases in effect at the time of death. The external death rates for the United States white male population were from an updated version of the Monson Program (3).

A modified life-table approach was used to calculate summary standardized mortality ratios. Ninety-five per cent confidence limits were determined using the programs of Rothman and Boice (4). Internal mortality comparisons were based on an approach that allowed for control by stratification of socioeconomic status, age at entry, and interval since entry into the study (5). The analysis thus adjusts for the potential influence of two correlates of the "healthy worker selection" effect (6, 7), namely, age at entry and interval since entry, and overcomes Miettinen's objections to the direct comparison of standardized mortality ratios (8). In principle, the method combines information across strata in a manner analogous to Mantel and Haenszel (9). The difference is that a multinomial instead of the hypergeometric distribution applies within strata, under the assumption that the proportional distribution of observed deaths within a stratum is the same as the proportional distribution of expected deaths within that stratum where the expected deaths are computed using external death rates and the modified life-table method. The test statistic is described in the Appendix. Because the statistic is based on large sample approximation theory, results must be interpreted cautiously when the observed number of deaths is small. Differences were described as significant if a two-tailed test yielded $p < 0.05$.

The vital and employment status of the study cohort is summarized in table 1 by company location and socioeconomic category at entry. Of the 1,919 employees, 1,648 (86 per cent) were employed in either the Pittsburg or Walnut Creek facilities, with the remaining group being located in Torrance, California. Two socioeconomic status (SES) levels were established, based on occupation at entry to the study; 443 men

TABLE 1

Vital and employment status of cohort by location and socioeconomic status (SES) as of December 31, 1979: study of employee mortality in chemical manufacturing

Location*	Total	Still employed	Retired	Deceased (company records)	Left before retirement		
					Deceased	Known alive	Unknown vital status
Total	1,919	529	152	231	159	734	114
Location 1	1,648	436	143	221	151	606	91
SES I†	417	140	26	34	30	167	20
SES II‡	1,231	296	117	187	121	439	71
Location 2	271	93	9	10	8	128	23
SES I	26	13	2	2	0	8	1
SES II	245	80	7	8	8	120	22

* Location 1, Pittsburg, CA; location 2, Torrance, CA.
† SES I, managers, supervision, professional.
‡ SES II, tradesmen, technicians, operators, service, and other.

designated "SES I" in the tables, were employed as managers, supervisors or professionals (chemists, engineers, etc.). Most of these men were college graduates. The second socioeconomic group, designated "SES II" in the tables, included 1,476 tradesmen, technicians, operators, service, and unskilled employees. The study cohort was Predominately white (93.4 per cent), with the remaining race or ethnic groups being Spanish-American (4.7 per cent), black (1.0 per cent), and Oriental (0.8 per cent).

During the course of follow-up, 529 men (27.6 per cent) remained employed, 152 men (7.9 per cent) had retired and were living, 231 men (12.0 per cent) had died while still an employee or following retirement from the company, and 1,007 men (52.5 per cent) left employment before retirement. Of this latter group of men, 734 were known to be alive, 159 were known to be deceased, and the vital status of 114 men was unknown as of December 31, 1979. The 114 men (5.9 per cent of the total cohort) were treated as lost to follow-up as of their company termination date. These men were similar to the total cohort in race and socioeconomic category, but tended to be younger and to have been hired more recently (43 per cent were hired during the 1940s compared with 27 per cent for the total cohort). Underreporting of deaths in Social Security files has been noted beginning in December 1977 for men who were employed at the time of death (10). A review of observed and expected deaths for 1978–1979 among employees under age 65 and who were not followed through company records did not reveal an important underreporting problem in this study. There were seven observed and 11.1 expected deaths.

The distribution of employees by date of hire, age at hire, and vital status outcome is given in table 2. Two-hundred-fifty-six of the men were hired prior to 1940; thus, their inclusion in the cohort occurred because they remained on the payroll as of January 1, 1940. The only unusual feature of the age-at-hire distribution was the older age of employees hired during the 1940–1949 period. This feature was particularly evident during 1940–1944 and probably reflects the limited availability of manpower during war years. Professional and supervisory personnel were older at hire than other employees (27.5 per cent were under 25 years of age, whereas 45.1 per cent of all other employees were under age 25 at hire). In part, this was due to transfers of professional employees from other company locations, the transfer date being treated as a new hire date.

TABLE 2

Distribution of 1,919 employees in cohort by date of hire, age at hire, and vital status outcome: study of [illegible] mortality in chemical manufacturing

Date of hire and age at hire (years)	Vital status as of Jan. 1, 1980				
	Total	Living	Unknown	Deceased	% deceased
Hired prior to 1940					
17–24	116	87	1	28	24.1
25–34	87	32	1	54	62.1
35–44	36	5	1	30	83.3
45+	17	2	1	14	82.4
Total	256				
Hired 1940–1949					
17–24	252	200	23	29	11.5
25–34	250	192	6	52	20.8
35–44	117	63	1	53	45.3
45+	84	15	2	67	79.8
Total	703				
Hired 1950–1959					
17–24	149	129	12	8	5.4
25–34	210	181	17	12	5.7
35–44	65	45		20	30.8
45+	19	11		8	42.1
Total	443				
Hired 1960–1969					
17–24	271	241	27	3	1.1
25–34	192	167	18	7	3.6
35–44	36	30	4	2	5.6
45+	18	15		3	16.7
Total	517				

As expected, deaths occurred most frequently among older employees hired earliest in time. Nearly 84 per cent of the observed deaths were among men hired prior to 1950. Thus, the summary measures give much more weight to the mortality experience of these men.

A brief characterization of the eight employment categories is provided in table 3. The first four categories are comprised of specific chemical manufacturing operations, the remaining categories cover miscellaneous production units or nonchemical-specific work activities that make up the balance of assignments at these locations. Each of the four major production units began operations prior to 1950. Because of job transfers within the company division, employees were assigned to an average of 1.5 different employment categories for periods of one year or more over the course of their company career. An individual was counted with each employment category to which he had been assigned.

RESULTS

Observed and expected deaths by [illegible] are summarized for the total cohort in table 4. For 10 decedents, cause of death information was lacking; these deaths were not apportioned to specific cause of death categories. The standardized mortality ratio for deaths due to all causes was 78 (95 per cent confidence interval: 71–86). Observed deaths were less than expected for most causes of death listed in table 4, and no individual causes of death were significantly elevated. A twofold nonsignificant increase was observed for leukemia (7 observed versus 3.8 expected deaths). Four of the leukemias were of the chroni[illegible]

TABLE 3

...scriptions and number of men by length of employment and year first employed for each employment category: study of employee mortality in chemical manufacturing

Title and description*	First assignment date	Employment duration (years)	
		1–4	5+
...rinated methanes production: 226 men assigned to a unit that produced various chlorinated hydrocarbons including the four chlorinated methanes and, more recently, perchloroethylene	pre-1950	86	51
	1950–1959	35	16
	1960+	33	5
...thates production: 178 men assigned to a unit that produced xanthates (e.g., sodium ethyl xanthate)	pre-1950	75	66
	1950–1959	26	0
	1960+	6	5
...onine production: 93 men assigned to a unit that produced methionine	pre-1950	13	4
	1950–1959	23	33
	1960+	18	2
...mic chemical production: 521 men assigned to units producing chlorine and caustic from brine as well as an ammonia production unit	pre-1950	169	174
	1950–1959	64	57
	1960+	43	14
...laneous small production units: 273 men assigned to various small production units of less than 100 men each	pre-1950	21	13
	1950–1959	22	45
	1960+	118	54
...nance and construction: 346 trademen such as boilers, painters, etc.—duties assigned throughout all operations of company division	pre-1950	26	99
	1950–1959	25	75
	1960+	67	54
...ch: 434 researchers and support personnel (e.g., laboratory technicians) assigned to central research laboratories	pre-1950	43	52
	1950–1959	74	72
	1960+	104	89
...tion, services, business: 899 men assigned to production crew, various service departments, and clerical and other business personnel	pre-1950	144	165
	1950–1959	119	141
	1960+	213	117

...the average each employee worked in 1.5 (2,970/1,919) different employment categories for 1+ years.

...type, two were acute myelogenous, ...e each was unspecified myelogenous ...pecified chronic.

...ional factors examined for the total ...included socioeconomic status at en...ers of company employment (1–2 ...3–9 Years, and 10+ years) and as...nt in any of eight employment cat... Cause-specific comparisons were ...for all major disease categories with ...more deaths in the total cohort, and ...subcategories of digestive and res... cancer.

...ll mortality was somewhat higher ...the lower socioeconomic occupations (table 5), but there were significant differences only for deaths due to external causes and respiratory cancer. No significant differences in overall or cause-specific mortality were observed relative to years of total employment in the company division, controlling for socioeconomic status, age at entry, and interval since entry to the study (table 6). The standardized mortality ratios for deaths due to all causes were 74, 93, and 74 for the 1–2 years, 3–9 years, and 10+ years groups, respectively.

Mortality was then examined for eight employment categories using both external and internal comparison methods. The ex-

TABLE 4

Observed and expected deaths by cause among 1,919 men in cohort, 1940-1979: study of employee mortality in chemical manufacturing

Cause of death category	Observed deaths	Expected deaths*	SMR†	95% CI‡
All causes	390	499.0	78	71-86
Infective and parasitic diseases	6	8.7	69	25-151
Malignant neoplasms, total	75	93.6	80	63-100
Buccal cavity and pharynx	1	3.1	32	00-179
Digestive organs and peritoneum	26	27.4	95	62-139
Stomach	5	5.7	88	28-204
Colon and rectum	11	11.7	94	47-168
Pancreas	6	5.1	117	43-254
Respiratory system	24	30.1	80	51-119
Prostate	4	6.2	65	18-165
Urinary organs	4	5.2	77	21-197
Brain and other Darts of nervous system	0	2.9	00	00-128
Leukemia	8	3.8	209	90-413
Lymphatic and hematopoietic tissue except leukemia	2	5.5	37	04-132
Residual	6	9.5	63	23-137
Benign and unspecified neoplasms	0	1.3	00	00-279
Endocrine, nutritional and metabolic diseases	6	7.7	78	29-169
Diseases of the circulatory system	203	258.9	78	68-90
Ischemic heart disease	144	177.4	81	68-96
Cerebrovascular disease	24	35.6	68	43-100
Diseases of the respiratory system	19	28.3	67	40-105
Emphysema	10	9.7	103	50-190
Diseases of the digestive system	17	24.7	69	40-110
Cirrhosis of the liver	6	12.4	48	18-105
Gastric and duodenal ulcer	6	3.8	158	58-341
Symptoms, senility and ill-defined conditions	0	5.3	00	00-70
All external causes	42	51.0	82	59-111
Accidents	27	35.2	77	51-112
Suicide	8	11.7	69	30-135
Residual causes	12	19.4	62	32-108
Unable to locate death certificate	10			

* Expected deaths based on United States white male mortality.

† SMR, standardized mortality ratio.

‡ 95% confidence interval based on Fisher exact limits when observed deaths were less than 20 and approximate limits otherwise.

ternal comparisons are summarized for deaths due to all causes and malignant neoplasms in table 7. None of the standardized mortality ratios was above 100. Similar comparisons were made for all major causes of death with five or more observed deaths in the total cohort and for respiratory and digestive cancer. No significant elevations for any of these causes of death were observed in any employment category relative to the corresponding United States white male population.

The internal company comparisons contrasted three groups: 5+ years in employment category, 1–4 years in employment category, and not known to have worked in that employment category. Work assignments of less than one year were not coded and thus were unknown to the investigators. In addition to examining differences among the three groups, a linear trend component was computed assigning scores of 2, 1 and *0* for the three respective groups. Although detailed tables are available for all employment categories, only one is provided in the interest of brevity. The results in table 8 pertain to the 226 men assigned to chlorinated methanes production. A sig-

TABLE 5

Observed and expected deaths by socioeconomic status (SES) at entry and cause of death for total cohort, 1940–1979: study of employee mortality in chemical manufacturing

Cause of death category	Deaths by socioeconomic status at entry				p value‡
	SES I*		SES II†		
	Observed/ expected	SMR§	Observed/ expected	SMR	
All causes	66/101.7	65	3241397.3	82	0.090
Infective and parasitic diseases	0/1.6	00	6/7.0	86	0.205
Malignant neoplasms, total	10/19.1	52	65/74.4	87	0.140
Digestive organs and peritoneum	6/5.5	109	20121.9	91	0.724
Respiratory system	0/6.2	00	24/23.8	101	0.015
Endocrine, nutritional and metabolic diseases	1/1.6	63	5/6.1	82	0.972
Diseases of the circulatory system	42/52.1	81	161/206.7	78	0.694
Diseases of the respiratory system	2/5.7	35	17122.6	75	0.255
Diseases of the digestive system	1/5.2	19	16/19.5	82	0.128
All external causes	4/10.9	37	38/40.1	95	0.035
Residual causes	3/5.0	60	9120.7	43	0.738
Unable to locate death certificate	3		7		

* SES I, managers, supervision, professional.
† SES II, tradesmen, technicians, operators, service, and other.
‡ Probability of no difference between the two SES groups after stratification by duration of employment, age at entry, and interval since entry.
§ SMR, standardized mortality ratio.

TABLE 6

Observed and expected deaths by duration of employment and cause of death for total cohort, 1940–1979: study of employee mortality in chemical manufacturing

Cause of death category	Deaths by duration of employment						p value*
	1–2 years		3–9 years		10+ years		
	Observed/ expected	SMR†	Observed/ expected	SMR	Observed/ expected	SMR	
All causes	71/96.1	74	100/108.1	93	2191294.8	74	0.169
Infective and parasitic diseases	1/2.0	50	3/2.4	125	2/4.2	48	0.089
Malignant neoplasms, total	13/17.8	73	16119.0	84	46/56.8	81	0.957
Digestive organs and peritoneum	4/4.9	82	7/5.6	125	15116.9	89	0.754
Respiratory system	1/5.8	17	4/5.7	70	19118.5	103	0.392
Endocrine, nutritional and metabolic diseases	3/1.4	214	0/1.6	00	3/4.7	64	0.140
Diseases of the circulatory system	30/45.2	66	52/52.8	98	1211160.8	75	0.173
Diseases of the respiratory system	2/5.0	40	6/5.6	107	11/17.7	62	0.332
Diseases of the digestive system	4/5.1	19	2/5.5	36	11/14.0	79	0.390
All external causes	14/14.2	99	14/15.0	93	14/21.8	64	0.769
Residual causes	1/5.2	19	2j6.0	33	9/14.6	62	0.633
Unable to locate death certificate	3		5		2		

* Probability of no difference among the three duration groups after stratification by socioeconomic group, age at entry, and interval since entry.
† SMR, standardized mortality ratio.

nificant decline in overall mortality was observed with increased years of assignment in the area ($p = 0.029$); among the 5+ years group, only 13 deaths were observed compared with 23.7 expected deaths after internal adjustment. The expected number of deaths based on the corresponding United States white male death rates was 29.2.

A significant among-group difference was seen for deaths due to endocrine, nutritional, and metabolic diseases (p =

TABLE 7

Observed and expected deaths for all causes and total malignant neoplasms among men ever assigned to employment category for 1+ years: study of employee mortality in chemical manufacturing

Employment category	All causes			Total malignant neoplasms		
	Observed/ expected*	SMR‡	95% CI†	Observed/ expected	SMR	95% CI†
Total cohort	3901499.0	78	71–86	75193.6	80	63–100
Chlorinated methanes	42166.7	63	45–85	9113.0	69	32–132
Xanthates	57173.8	77	59–100	13113.8	94	50–161
Methionine	10120.4	49	24–90	3/4.0	74	15–217
Inorganic chemicals	138/167.5	82	69–97	29131.9	91	61–131
Miscellaneous small production units	33139.1	84	58–119	4/7.3	55	15–140
Maintenance	54173.9	73	55–95	14114.9	94	52–158
Research	51167.5	76	56–99	9113.2	68	31–129
Distribution, services, and business	1891233.3	81	70–93	30144.0	68	46–97

* Expected deaths based on United States white male mortality.

† 95% confidence interval based on Fisher exact limits when observed deaths were less than 20 and approximate limits otherwise.

‡ SMR, standardized mortality ratio.

TABLE 8

Observed and conditional expected deaths by cause and employment duration among men assigned to employment category I, chlorinated methanes production for 1+ years: study of employee mortality in chemical manufacturing*

Cause of death category	Deaths by duration of employment		Among-groups *p* value	Trend *p* value
	1–4 years Observed/ expected	5+ years Observed/ expected		
All causes	29130.0	13123.7	0.067	0.029†
Infectious and parasitic diseases	0/0.5	0/0.4	0.615	0.356
Malignant neoplasms, total	6/5.9	3/5.2	0.609	0.370
Digestive organs and peritoneum	4/1.7	2/1.6	0.170	0.243
Respiratory system	212.2	1/2.1	0.716	0.418
Endocrine nutritional and metabolic diseases	3/0.5	0/0.4	0.001	0.181
Diseases of the circulatory system	9/13.9	9112.4	0.201	0.110
Diseases of the respiratory system	2/1.4	1/1.4	0.834	0.982
Diseases of the digestive system	3/1.7	0/1.2	0.337	0.652
All external causes	4/4.7	0/1.9	0.334	0.168
Residual causes	1/0.7	0/0.6	0.693	0.561
Unable to locate death certificates	1			

* Expected deaths conditioned to equal observed deaths across total cohort: stratification by socioeconomic status, age at entry, and interval since entry.

† The mortality ratio declined with increased duration of employment.

0.001). Three of the six men in the total cohort whose deaths were due to these causes had been assigned to the chlorinated methanes area. All three of these deaths were due to diabetes mellitus and all three men had spent less than five years in the chlorinated methanes work area. It was also noted that three of the six digestive system malignancies within this employee subgroup were pancreatic cancers (0.9 expected deaths after internal adjustment). Two of these three men had worked for less than five years in the area and the third man for six years. Time-space clustering was apparent for each disease as the men in both case groups were first assigned to chlorinated

methanes production between 1942 and 1946 and none of the men remained in this work area after 1948. Two of the men were Spanish-Americans.

Internal comparisons for the xanthates and methionine production areas were unremarkable. Similar comparisons for the inorganic chemical production area revealed an among-group difference for diseases of the digestive system ($p = 0.034$), which was supported by a linear trend with increased employment duration ($p = 0.010$). This was based on six observed deaths (10.4 expected deaths after internal adjustment) among men not known to have worked in the area, three observed deaths (2.8 expected deaths after internal adjustment) among men in the 1–4-year duration group, and eight observed deaths (3.8 expected deaths after internal adjustment) among men in the 5+ years group. More specifically, the trend was due to increases in gastric and duodenal ulcer with zero, two, and four deaths for the three respective categories. On additional review of the six ulcer deaths, five were found to be gastric and one was duodenal in origin. Three of the men were identified as having worked in the caustic and brine section of inorganic chemical production for 5+ years and as having died between 1941 and 1953.

Internal comparisons for the category, miscellaneous small production units, revealed one significant finding: four deaths due to external causes among individuals in the 5+ years category (1.3 expected deaths after internal adjustment). Two of these deaths were due to automobile accidents and the other two to an in-plant explosion that occurred in 1971.

Among maintenance employees (tradesmen) there were no significant findings from the internal comparisons. However, there was a trend of increased respiratory cancer among men in the 5+ years category based on eight observed versus 4.0 expected deaths after internal adjustment ($p = 0.058$). One of these eight employees, who died at age 48, had been an insulator for 13 years. There were no notable job assignment patterns among the seven remaining men in this subgroup. Finally, no findings of occupational interest were noted among the 1) research and 2) distribution, services, and business groups.

Discussion

The chemical manufacturing and research operations covered in this study were diverse in nature, including both inorganic and organic chemical production. The facilities were, in general, modern in design. For example, most of the chemical processing is performed in open structures, thus providing better control of occupational exposures. The overall findings of favorable mortality relative to the corresponding United States population were consistent with those reported in a similar study of employees at another location of the company (11). The all causes standardized mortality ratio for the present study was 78 compared to 81 in the update of the Michigan location study (5). The low mortality in both groups relative to the United States white male population is presumably a reflection of 1) initial favorable selection into an employee population, 2) positive benefits from continued employment, and 3) the lack of major occupational health effects in the cohort.

There were no statistically significant elevations for any specific causes of death. A twofold increase in leukemia was observed for the cohort. However, the distribution of leukemia by type was not unusual (four lymphatic, three myelogenous, and one unspecified) and there was no concentration of deaths in any one employment category. Three leukemia deaths each were observed in the research and inorganic chemical production categories.

Comparisons between the socioeconomic groups revealed significant increases for respiratory cancer and all external causes of death in the lower socioeconomic group. These findings are consistent with mortality differentials seen in other similar stud-

ies (12) and with differences seen in smoking patterns by socioeconomic group (13).

There were several findings of interest relative to specific employment categories. For example, in the chlorinated methanes area, three deaths each were due to pancreatic cancer and diabetes. There was no apparent exposure-response effect for either disease; that is, only one of the six individuals had been assigned to that work area for 5+ years. There were, however, indications of a time-space cluster since the six men were hired between 1942 and 1946, were first assigned to the area within that same four-year period, and had all left the chlorinated methanes area by 1948. The ages of the cases were 56, 57, and 58 years for the diabetes deaths and 68, 76, and 90 for the pancreatic cancer deaths. Intervals between first assignment to the area and death were between 20 and 31 years. We are unaware of any toxicologic reports linking chlorinated methanes (methyl chloride, dichloromethane, chloroform, or carbon tetrachloride) with diabetes or pancreatic cancer. Insufficient information was available from the death certificates to subcategorize the diabetes deaths as to insulin-dependent or insulin-independent types. Review of company records did indicate that one of the men had been diabetic at hire in 1944, and that a second man had been very obese.

Limited epidemiologic evidence for a relationship between pancreatic cancer and dry cleaning (potential exposures include carbon tetrachloride in the past and tetrachloroethylene since the 1950s) was given by Lin and Kessler (14). However, this possible relationship has not been supported in three other studies specifically directed at dry cleaners (15–17). At present then, there appears to be no explanation for our observations.

A second finding was that of a relative increase in digestive system disease deaths among men assigned to the inorganic chemical production area compared with all other men in the study population. More to the point, gastric and duodenal ulcer deaths were increased (six observed versus 1.3 expected deaths), particularly in the 5+ years category (four observed versus 0.8 expected deaths). Five of the cases were assigned to the caustic and brine section, three for 5+ years. However, in a study of similar operations at another company location, there were no deaths due to gastric or duodenal ulcer (18). The inconsistency across studies and the lack of a biologic hypothesis detract from the importance of this finding.

The multiple internal comparisons yielded several statistically significant findings, but failed to reveal any cause-specific patterns of mortality demonstrative of an occupational effect except for two deaths caused by an in-plant explosion.

For the external comparisons, the probability of detecting a true difference is directly related to the number of expected deaths. With a two-tailed significance level of 0.05 and with 80 per cent power, a relative risk of 3 can be detected for any disease category in which expected deaths exceed 3.7 and a relative risk of 2 can be detected when expected deaths exceed 12.3 (19). Since the expected number of deaths exceeded 3.7 for most causes of death in the total cohort and for major cause of death categories in the employment subgroups, threefold or greater risks could be detected with reasonable power in such comparisons. For rare causes of death, however, even higher risk ratios than 3 would have a low probability of detection.

In evaluating both external and internal methods of analysis, it has been shown that the use of external controls increases power except when death rates in a study population are substantially lower than in the comparison population, as occurs in comparing an industrial to a general population (20). In this situation the reverse can be demonstrated. In the present study the internal method of analysis appears to be more sensitive in detecting differences than the external method, simply based on the number of significant differences found in

the comparisons. This would be anticipated among causes of death for which mortality deficits exist at the total cohort level and where a trend analysis allows an additional dimension of comparison. The internal analyses also have the advantage of eliminating other potential sources of confounding, such as location of residence.

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APPENDIX

The test statistic used in internal comparisons may be formulated by considering the ith stratum and generalizing the statistic across strata *(5)*. For $j = 1, 2, \ldots, s$ subcohorts from which comparisons are to be made, one has within the ith stratum

	Subcohort						Total
	1	2	...	j	...	s	
Observed deaths	O_{i1}	O_{i2}	...	O_{ij}	...	O_{is}	$\sum_J O_{ij}$
Expected deaths	E_{i1}	E_{i2}	...	E_{ij}	...	E_{is}	$\sum_I E_{ij}$

where expected deaths are computed in standard fashion from age- and era-specific death rates (for the United States white male population). Because strata are defined by age at entry and interval since entry categories, the person-years within any given stratum will necessarily cover a narrow age and calendar period range. Taking the observed deaths in the ith stratum and jth subcohort, O_{ij}, to be Poisson distributed and assuming the null hypotheses of no differences in proportional hazard among the subcohorts (i.e., assuming observed deaths in the ith subcohort to be in the same proportion to total deaths within

the stratum as expected deaths in that subcohort to total expected deaths in the stratum), the conditional distribution of observed deaths is multinomial with parameters

$$N_i = \sum_J O, \quad \text{and} \quad \pi_{ij} = E_{ij} / \sum_J E_{ij}.$$

Combining results across strata yields a large sample test statistic

$$\chi^2_{s-1df} = \text{DIF COV}^{(-)} \text{DIF}'$$

where DIF is a 1 × s matrix of observed less conditional expected deaths with elements

$$\left[\sum_i (O_{i1} - N_i\pi_{i1}), \sum_i (O_{i2} - N_i\pi_{i2}), \ldots, \sum_i (O_{is} - N_i\pi_{is})\right],$$

$\text{COV}^{(-)}$ is the generalized inverse of the s × s summary covariance matrix COV, COV having diagonal elements

$$\sum_i N_i\pi_{ij}(1 - \pi_{ij})$$

and off-diagonal elements of

$$-\sum_i N_i\pi_{ij}\pi_{ij'} \quad \text{for} \quad j \neq j'.$$

For descriptive purposes, the conditional expected number of deaths in the jth subcohort is

$$\sum_i N_i\pi_{ij}.$$

Specific linear and interaction contrasts can be tested by introducing a design matrix X such that

$$\chi^2 = \text{DIF X}' \ (\text{X COV } X')^{(-)} \text{ X DIF}'$$

with degrees of freedom equal to the rank of X.