

15. Dukes, M.N.G. *Meyler's Side Effects of Drugs*. Volume 8. 1975. Excerpta Medica, Amsterdam-Oxford, American Elsevier Publishing Co. Inc., N.Y. (and Annuals 1 and 2, published 1977 and 1978).
16. Ognibene, A.J. Agranulocytosis due to dapson. *Ann. Int. Med.* 72:521. 1970
17. *AMA Drug Evaluations* - Fourth Edition. John Wiley & Sons. 1980
18. Goodman, L.S; Gilman, A. *Pharmacological Basis of Therapeutics*. Sixth Edition. Macmillan Publishing Co. 1980.
19. Centers for Disease Control Morbidity and Mortality Report. Revised recommendations for malaria prophylaxis for travelers to East Africa; 1982 (June 25); Vol. 31/No. 24:328-30
20. Kihamia CM, Gill HS. Chloroquine resistant *Falciparum* malaria in semi-immune native African Tanzanians. *Lancet* 1982 2:43

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EPIDEMIOLOGIC STUDY OF REFINERY AND CHEMICAL PLANT WORKERS

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A dynamic retrospective cohort study was performed to examine the mortality experience of workers at Exxon's Baton Rouge, La., refinery and chemical plant. Included were 8,666 regular employees who worked at least one month during the period Jan. 1, 1970, through Dec. 31, 1977, and retirees who were alive as of Jan. 1, 1970. Mortality from all causes of death was lower than expected when compared with that of the U.S. population of similar age, sex, and race. Analyses of mortality by specific site of cancer revealed elevated standardized mortality ratios (SMRs) for cancer of the kidney, testis, brain/central nervous system, pancreas, and lymphoplastic sites; none of these elevations was statistically significant. Because of the higher than average mortality from cancer of the pancreas in some Louisiana parishes and the observation that one additional death from cancer of the pancreas in this study would have resulted in a statistically significant SMR at the 95% confidence level, some emphasis was placed on this finding. No evidence was found to link cancer of the pancreas to a specific occupational group. An examination of mortality by occupational class revealed some elevated SMRs for further study.

Early epidemiologic studies of petrochemical industry employees, published before 1970, indicated no association between diseases and

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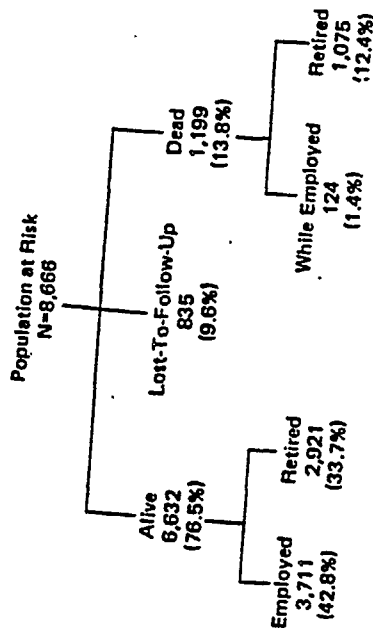


occupational exposures.¹⁻³ Among those published since 1970, some have shown more cancers of the lung and bladder than were expected.⁴⁻⁹ More recent studies have had varied results as well. In a study performed for the American Petroleum Institute, more deaths were observed from lymphomas and cancer of the genitalia than were expected based on death rates for U.S. men in similar age groups.¹⁰ A standardized proportional mortality study of the refinery and petrochemical plant workers of the Oil, Chemical and Atomic Workers International Union showed among white males a larger proportion of deaths than expected for all malignant neoplasms.¹¹ Examination of specific sites indicated cancer of the digestive and respiratory tracts, skin, and brain were major contributors to this increased proportion. Separate examination of cancer of the pancreas by length of union membership showed a greater than expected proportion among those with less than ten years' membership but no difference for those with membership for more than ten years. A study of workers at a Canadian refinery found that standardized mortality ratios (SMRs) for cancer of the brain and digestive system were elevated, but the increases were not statistically significant.¹² A study of the male employees of another Canadian petroleum and petrochemical company showed a statistically significant increase in the number of deaths among hydrocarbon-exposed persons as compared with a group of nonexposed controls.¹³ The numbers of cancers of the esophagus and stomach and of the trachea, bronchus, and lung in the exposed group were greater than expected on the basis of comparison with the nonexposed controls. Comparisons between the refinery and nonrefinery groups indicated an increased risk among refinery workers for total malignant neoplasms and for cancer of the intestinal tract.

The many differences among these studies may be due to variations in the study designs, in the populations included, and in the analytical methods used. There is a need for additional examination of other available populations with the potential for similar kinds of occupational exposure to determine whether any of these findings can be replicated.

A cohort of workers from Exxon's Baton Rouge refinery and chemical plant was selected for a mortality study. The purpose of this study was to ascertain whether the mortality experience observed in the cohort would be the same as or different from that expected based on the U.S. age-, sex-, and race-specific death rates for major causes of death and selected sites of cancer.

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Materials and Methods

Study Design and Population Definition - A retrospective cohort study design was used to examine the mortality experience of workers at Exxon's Baton Rouge refinery and chemical plant. The study population included all regular refinery and chemical plant employees who worked at the Baton Rouge site for at least one month during the eight-year period, Jan. 1, 1970, through Dec. 31, 1977, and retirees who were alive as of Jan. 1, 1970. The total study population numbered 8,666. This population was dynamic, with individuals entering the 1970 to 1977 observation period at various times and remaining for varying periods. The Figure above details the population at risk by vital status category as of the end of the study period; 6,632 were known to be alive, 1,199 were known to be dead, and the vital status of 835 (9.6% of the total study population) was unknown. The group with unknown vital status comprised transferees and employees who terminated employment during the study period; for analysis they were considered lost-to-follow-up and were included in the calculation of person-years until they terminated. Over 85% of this lost-to-follow-up group was under 40 years of age at last observation, and 77% had five years or less of employment at the time of termination. Lack of vital status information for the lost-to-follow-up group is not likely to have biased the mortality ratios significantly, since mortality (particularly that due to cancer) is low in these younger age groups. If the persons lost to follow up had not been lost, they would have contributed

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categories used were as follows: official/manager, professional, technician, office worker/clerk, mechanic, process operator, unskilled laborer, and service worker.

The underlying cause of death was coded by a trained nosologist according to the eighth revision of the International Classification of Diseases.¹⁴ Ninety-nine percent of the death certificates were available. The data were entered and stored on computer. Errors in data consistency and value ranges were identified and corrected.

Data Analysis - A computer software package (Statistical Analysis System) developed at North Carolina State University is used to identify data errors and to produce frequency distributions to describe the population. A computer program developed by

Table 2 -- Population at Risk by Beginning Year of Employment in Five-Year Groups, 1970-1977		
Beginning Year of Employment (5-yr Groups)	No.	Frequency, %
pre-1915	86	1.0
1915-1919	333	3.8
1920-1924	487	5.6
1925-1929	441	5.1
1930-1934	148	1.7
1935-1939	618	7.1
1940-1944	2,093	24.2
1945-1949	803	9.3
1950-1954	275	3.2
1955-1959	51	0.6
1960-1964	95	1.1
1965-1969	1,244	14.4
1970-1974	1,339	15.5
1975-1977	648	7.5
Subtotal		
Known	8,661	
Unknown	5	
Total	8,666	

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Table 1 -- Population at Risk by Age at Last Observation
and by Sex and Race (Total = 8,666)

Age, yr	Male			Female		
	White*	Black		White*	Black	
	No.	(%)	No. (%)	No.	(%)	No. (%)
<20	19 (0.2)	3 (...)	0 (...)	0 (...)	0 (...)	0 (...)
20-24	354 (4.3)	114 (1.4)	73 (16.6)	22 (5.0)	22 (5.0)	22 (5.0)
25-29	895 (10.9)	269 (3.3)	62 (14.0)	34 (7.7)	34 (7.7)	34 (7.7)
30-34	718 (8.7)	144 (1.8)	40 (9.1)	10 (2.3)	10 (2.3)	10 (2.3)
35-39	316 (3.8)	48 (0.6)	17 (3.9)	2 (0.5)	2 (0.5)	2 (0.5)
40-44	138 (1.7)	11 (0.1)	9 (2.0)	1 (0.2)	1 (0.2)	1 (0.2)
45-49	134 (1.6)	1 (...)	11 (2.5)	0 (...)	0 (...)	0 (...)
50-54	465 (5.7)	8 (0.1)	34 (7.7)	0 (...)	0 (...)	0 (...)
55-59	699 (8.5)	62 (0.8)	37 (8.4)	0 (...)	0 (...)	0 (...)
60-64	859 (10.4)	118 (1.4)	34 (7.7)	0 (...)	0 (...)	0 (...)
65-69	771 (9.4)	163 (2.0)	23 (5.2)	1 (0.2)	1 (0.2)	1 (0.2)
70-74	656 (8.0)	151 (1.8)	17 (3.9)	1 (0.2)	1 (0.2)	1 (0.2)
75-79	495 (6.0)	93 (1.1)	7 (1.6)	0 (...)	0 (...)	0 (...)
80-84	283 (3.4)	70 (0.9)	4 (0.9)	0 (...)	0 (...)	0 (...)
>84	127 (1.5)	41 (0.5)	1 (0.2)	0 (...)	0 (...)	0 (...)
Total	6,929 (84.2)	1,296 (15.8)	369 (83.7)	72 (16.3)	72 (16.3)	72 (16.3)

* Includes minorities other than black

additional person-years to the denominator; this small increase would not have been likely to affect the overall results.

Data - Extracts from company personnel files and medical records provided the following information for each member of the study population: social security number, company identification number, name, date of birth, sex, race, date of employment, date of termination, work-history summaries, status at last observation, date of death, underlying cause of death, and, when available, a history of smoking and alcohol consumption.

Work histories were summarized to derive the occupation and department or unit where each employee spent the largest portion of his working time at the Baton Rouge site. The occupational

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Monson¹⁶ was used to calculate SMRs, adjusted for age, sex, race, and calendar year, using the U.S. death rates as the standard. The rates for age and calendar year were in five-year groupings. To be consistent with the criteria employed in calculating the U.S. rates, minorities other than black in the study population were included with the white subgroup. The 95% confidence intervals were calculated, based on a ratio of a variable to its expectation, assuming a Poisson distribution.¹⁷ The SMRs were calculated for the total population at risk, for occupational classes, and for employees hired before 1956, to allow for a latency effect, if any, to be detected.

Table 3 - The Distribution of Deaths by Major Cause in the Study Population

Major Cause of Death	Observed Deaths	
	No.	(%)
Infective and parasitic diseases (001-136)*	5	(0.4)
Neoplasms (140-239)	252	(21.0)
Endocrine, nutritional, and metabolic diseases (240-279)	18	(1.5)
Diseases of blood and blood-forming organs (280-289)	6	(0.5)
Mental disorders (290-315)	1	(0.1)
Diseases of CNS (320-389)	7	(0.6)
Diseases of circulatory system (390-458)	728	(60.7)
Diseases of respiratory system (460-519)	65	(5.4)
Diseases of digestive system (520-577)	35	(2.9)
Diseases of genitourinary system (580-629)	25	(2.1)
Diseases of skin and subcutaneous tissue (680-709)	1	(0.1)
Diseases of musculoskeletal system and connective tissue (710-738)	2	(0.2)
Symptoms, senility and ill-defined conditions (780-796)	5	(0.4)
All external causes (800-999)	49	(4.1)
Total Observed	1,199	(100.0)

* International Classification of Diseases¹⁴ codes, eighth revision (1967) shown in brackets

Results

Population Description - Table 1 describes the population at risk by age at last observation and by sex and race. The age distribution is bimodal, with peaks at ages 25 to 29 and 60 to 64. About 60% of the population was male. There were more women in the younger than in the older age groups. Blacks accounted for approximately 16% of the population. Table 2 gives the distribution of the study population by beginning year of employment. About 50% of the population began employment before 1945. The occupational categories were distributed in the following way: operators, mechanics, and laborers (72.5%); all other (25.9%); unknown (1.6%). Of the operators, mechanics, and laborers group, 32% were operators, 60% were mechanics, and 8% were laborers.

Mortality Analysis - The distribution of deaths by major cause in the population at risk is given in Table 3. Sixty-one percent died of diseases of the circulatory system and 21% from neoplasms. Of the 252 neoplasms, 249 were known to be malignant.

Table 4 gives the SMRs for the major causes of death for the population at risk. The SMR for all causes of death was 92 (95% confidence interval, 87 to 97), a finding significantly lower than

Table 4 - Standardized Mortality Ratios (SMRs) for Major Causes of Death for the Population at Risk, 1918-1977			
Cause of Death	Obs/Exp*	SMR (N)	95% CI†
All causes of death (001-999)	1199/1309.3	92	87-97
Infective and parasitic diseases (001-136)	5/9.8	51	17-119
Malignant neoplasms (140-239)	249/210.4	92	81-104
Benign neoplasms (240-279)	3/2.6	115	24-326
Endocrine, nutritional, and metabolic diseases (240-279)	18/24.4	74	44-117
Diseases of blood and blood-forming organs (280-289)	6/2.2	222	81-486
Mental disorders (290-315)	1/6.9	151	0-94
Diseases of CNS (320-389)	7/2.1	72	31-159
Diseases of circulatory system (390-458)	728/723.1	101	94-109
Diseases of respiratory system (460-519)	65/92.1	71	55-91
Diseases of digestive system (520-577)	35/49.5	71	49-98
Diseases of genitourinary system (580-629)	25/19.8	126	81-188
Diseases of skin and subcutaneous tissue (680-709)	1/1.1	91	2-508
Diseases of musculoskeletal system and connective tissue (710-738)	2/2.2	91	11-329
Symptoms, senility and ill-defined conditions (780-796)	5/19.3	261	8-61
All external causes (800-999)	49/18.6	263	47-49
Total	Person-years 92,791.3 No. of employees 8,586 No. of deaths 1,199		

* Expected (Exp) deaths based on age, sex, race, and cause specific U.S. population rates calculated for each five year calendar period; Obs indicating observed deaths

† International Classification of Diseases, eighth revision codes shown in brackets; CI is confidence interval

‡ The SMR is statistically significant at $p < .05$ if CI does not include 100

expected. The SMRs for deaths due to mental disorders, diseases of the respiratory tract and digestive systems, ill-defined conditions, and all external causes were significantly lower than expected. The SMRs for deaths due to benign/unspecified neoplasms and to diseases of the blood and circulatory and genitourinary systems were elevated, but not enough to be statistically significant.

The SMRs for deaths due to malignant neoplasms in the population at risk are given in Table 5. Deaths due to all cancers (SMR=92) and to cancers of the majority of individual sites were fewer than expected, while those due to cancers of the pancreas (SMR=152), the testis/other genitalia (SMR=222), the kidney (SMR=155), the brain/central nervous system (CNS) (SMR=102), and other secondary and unspecified sites (SMR=113), to lymphoreticular sarcoma (SMR=119) and to cancers of all lymphoproliferative sites (SMR=109) were slightly elevated. One statistically significant

Table 5 - Standardized Mortality Ratios (SMRs) for Deaths From Malignant Neoplasms for Population at Risk, 1970-1977

Cancer Death Site	Obs/Exp ^a	SMR (%)	95% CI ^b
All malignant neoplasms (148-209) ^c	240/270.4	92	81-104
Buccal cavity/pharynx (148-149)	2/17.6	291	3-344
All digestive organs (148-156)	75/74.9	97	76-122
Esophagus (150)	7/72.5	95	39-196
Stomach (151)	17/121.7	90	49-143
Large intestine (153)	24/25.1	95	62-131
Rectum (154)	3/73.9	38	8-111
Liver, gallbladder, bile ducts (155, 156)	3/4.5	67	14-196
Pancreas (157)	23/15.1	152	88-276
Respiratory system (160-163)	78/85.3	91	72-114
Lung (162)	4/5.1	78	21-199
Bronchus, connective tissue, other, trachea (170-174)	39/44.5	88	62-120
All genitourinary organs (166-169)	19/28.6	66	48-86
Prostate (165)	2/0.9	222	27-401
Testis/other genitalia (168)	8/9.2	88	45-168
Bladder (169)	8/5.8	135	31-259
Kidney (167)	5/4.3	102	32-239
Brain/CNS (181-192)	22/19.4	113	71-171
Other, secondary, and unspecified sites (195-199)	35/23.0	151	78-281
All lymphoproliferative sites (200-208)	54/4.2	129	32-278
Lymphoreticular neoplasms (200)	9/9.3	97	41-184
Leukemia (204-207)	17/2.2	87	28-209
Other lymphoproliferative sites (201, 205, 208)	17/2.2	87	28-209
Total	92,781.3	92	78,119
Person-years	9,458		
No. of deaths	1,199		
No. of cancer deaths	249		

^a Expected (Exp) deaths based on age, sex, race, and cause-specific U.S. population rates calculated for each five-year calendar period; Obs is observed deaths.

^b The SMR is statistically significant at $p < 0.05$ if confidence interval (CI) does not include 100.

^c International Classification of Diseases (ICD-9), eighth revision codes shown in brackets.

^d The SMRs were not calculated for sites with only one observed death; these were: larynx, small intestine, peritoneum, and Hodgkin's disease; expected values for ICD-9 code 205 (lymphoproliferative) and included in the all lymphoproliferative total.

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Table 6 - Standardized Mortality Ratios (SMRs) for Deaths by Cause and by Occupational Category 1970-1977

Cause Site	Occupational Category ^a				All SMR (%)	95% CI ^b
	Obs/Exp ^c	SMR (%)	95% CI ^b	Obs/Exp ^c		
All malignant neoplasms (148-209) ^c	240/270.4	92	81-102	405/315	781	54-95
Buccal cavity/pharynx (148-149)	2/17.6	291	3-344	4/122	65	31-119
All digestive organs (148-156)	75/74.9	97	76-122	107/104	103	85-122
Esophagus (150)	7/72.5	95	39-196	10/104	96	48-161
Stomach (151)	17/121.7	90	49-143	10/104	96	48-161
Large intestine (153)	24/25.1	95	62-131	10/104	96	48-161
Rectum (154)	3/73.9	38	8-111	10/104	96	48-161
Liver, gallbladder, bile ducts (155, 156)	3/4.5	67	14-196	10/104	96	48-161
Pancreas (157)	23/15.1	152	88-276	10/104	96	48-161
Respiratory system (160-163)	78/85.3	91	72-114	10/104	96	48-161
Lung (162)	4/5.1	78	21-199	10/104	96	48-161
Bronchus, connective tissue, other, trachea (170-174)	39/44.5	88	62-120	10/104	96	48-161
All genitourinary organs (166-169)	19/28.6	66	48-86	10/104	96	48-161
Prostate (165)	2/0.9	222	27-401	10/104	96	48-161
Testis/other genitalia (168)	8/9.2	88	45-168	10/104	96	48-161
Bladder (169)	8/5.8	135	31-259	10/104	96	48-161
Kidney (167)	5/4.3	102	32-239	10/104	96	48-161
Brain/CNS (181-192)	22/19.4	113	71-171	10/104	96	48-161
Other, secondary, and unspecified sites (195-199)	35/23.0	151	78-281	10/104	96	48-161
All lymphoproliferative sites (200-208)	54/4.2	129	32-278	10/104	96	48-161
Lymphoreticular neoplasms (200)	9/9.3	97	41-184	10/104	96	48-161
Leukemia (204-207)	17/2.2	87	28-209	10/104	96	48-161
Other lymphoproliferative sites (201, 205, 208)	17/2.2	87	28-209	10/104	96	48-161
Total	92,781.3	92	78,119	13,228.3	2,243	48
Person-years	9,458			9,458		
No. of deaths	1,199			1,199		
No. of cancer deaths	249			249		

^a Excludes 147 workers with missing work histories; of these, 31 were decedents (these cancer deaths).

^b Expected (Exp) deaths based on age, sex, race, and cause-specific U.S. population rates calculated for each five-year period; Obs is observed deaths.

^c The SMR is statistically significant at $p < 0.05$ if confidence interval (CI) does not include 100.

^d International Classification of Diseases (ICD-9), eighth revision codes shown in brackets.

^e The SMRs were not calculated for sites with only one observed death; these were: larynx, pancreas, and Hodgkin's disease (all in the genitourinary category); expected values for ICD-9 code 205 (lymphoproliferative) and included in the all lymphoproliferative category; are not shown separately.

difference ($p < 0.05$) was observed, namely, in the reduced mortality from cancer of the buccal cavity and pharynx (SMR=26). One probable death due to cancer of the pancreas could not be coded as such because of the cause of death wording on the death certificate that referred to this as a tumor, not necessarily malignant. If it had been, the resulting pancreatic cancer SMR of 159 would be statistically significant at $p < 0.05$.

Standardized mortality ratios for cancer death by anatomic sites were calculated for the subgroup of operators, mechanics, and laborers (a total of 6,281 individuals contributing 38,960 person-years), a group more likely to be in contact with petroleum and its derivatives. These are given in Table 6. Elevated but not statistically significant SMRs were observed for all cancers of the digestive tract, for cancer of the esophagus, large intestine, pancreas, bladder, testis/other genitalia, kidney, and brain/CNS, for

lymphoreticular sarcoma, for cancer of other lymphatic tissues, and for all lymphopneitic cancers. Total cancer mortality (SMR=98) showed no difference from that of the U.S. population. In the "all other" occupational category (2,243 individuals contributing 13,230 person-years), elevated but not statistically significant SMRs were observed for cancer of the pancreas and bone, connective tissues, skin, and breast. The total cancer mortality (SMR=70) was significantly lower than expected in this group. Since the SMR calculation employs an indirect method of standardization, it is inappropriate to compare these occupational subgroups directly.¹⁸

The SMRs were calculated for the 5,297 employees hired before 1956, that is, those with 15 or more years of employment. This subgroup contained 61% of the total population at risk and contributed 71% of the person-years. The total number of deaths for this group was 1,180, or 98.4% of all cohort deaths.

Table 7 - Standardized Mortality Ratios (SMRs) for Major Causes of Death Among Employees Hired Before 1956, 1970-1977 Cohort

Cause of Death	Obs/Exp ^a	SMR (95% CI) ^b
All causes of death (201-899)	1180/1271.5	93
Infective and parasitic diseases (001-133)	5/0.6	82
Malignant neoplasms (140-209)	247/258.9	95
Benign neoplasms (210-239)	32/5.5	58
Endocrine, nutritional, and metabolic diseases (240-279)	102/23.9	75
Diseases of blood and blood-forming organs (280-289)	62/5.5	23
Mental disorders (290-319)	17/1.1	15
Diseases of circulatory system (320-389)	78/5.5	82
Diseases of respiratory system (400-479)	728/717.3	101
Diseases of digestive system (500-579)	64/91.8	70
Diseases of genitourinary system (580-639)	34/47.7	71
Diseases of skin and subcutaneous tissue (640-689)	25/19.5	128
Diseases of musculoskeletal system and connective tissue (700-799)	17/1.1	91
Diseases of nervous system and sense organs (800-899)	21/2.1	85
Symptoms, signs, and ill-defined conditions (900-999)	518/2.2	231
All external causes (000-099)	34/54.8	62
Total	Person-years 37,425 No. of employees 5,297 No. of deaths 1,180	

^a Expected (Exp) deaths based on age, sex, race, and cause-specific U.S. population rates calculated for each five year calendar period. Obs is observed deaths.

^b The SMR is statistically significant at $p < 0.05$, if confidence interval (CI) does not include 100.

^c International Classification of Diseases, eighth revision codes shown in brackets.

Table 7 gives the SMRs for the major causes of death; SMRs for malignant neoplasms by specific sites are shown in Table 8; and Table 9 gives the SMRs for malignant neoplasms by occupational class for the pre-1956 group. All of these results were very similar to those for the total 1970 to 1977 cohort.

Discussion

The mortality of the employee population at Exxon's Baton Rouge refinery and chemical plant during the period 1970 to 1977 was generally less than expected when compared with that of the U.S. population in similar age, sex, and race categories. This was also true for workers employed for 15 or more years. Such a finding is common among studies of employed populations and has been labeled the "healthy worker effect."¹⁹ The usual explanation for the phenomenon is that healthier people are selected into and remain members of the work force. However, this type of selection is not likely to be an important factor in chronic diseases with long latency periods, such as cancer,^{19,20} the major focus of this study.

Other investigators⁶⁻¹³ have observed higher than expected mortality from cancer of certain sites, namely, the lung, esophagus, stomach, intestines, and bladder, and from lymphomas among

Table 8 - Standardized Mortality Ratios (SMRs) for Deaths From Malignant Neoplasms Among Employees Hired Before 1956, 1970-1977 Cohort

Cause of Death	Obs/Exp ^a	SMR (95% CI) ^b
All malignant neoplasms (140-209)	247/258.9	95
Rectal cancer (pharynx) (140-149)	2/7.6	26
All digestive organs (150-159)	73/74.6	98
Esophagus (150)	7/2.2	31
Stomach (151)	21/19.6	107
Large intestine (152)	24/24.9	96
Rectum (154)	3/7.8	38
Liver, gallbladder, bile ducts (155, 156)	3/4.4	68
Pancreas (157)	23/15.0	153
Lung (162)	78/64.7	120
Bronch, connective tissue, etc., trachea (170-174)	78/64.7	120
All genitourinary organs (180-189)	33/44.1	75
Prostate (185)	19/28.5	67
Bladder (188)	3/5.1	59
Kidney (189)	8/5.8	135
Brain/CNS (191-192)	4/4.6	87
Other, secondary and unspecified sites (193-199)	22/18.1	122
Lymphopneitic (200-209)	25/22.1	113
Lymphoreticular neoplasms (200)	5/4.1	122
Leukemia (204-207)	9/9.1	99
Other lymphatic tissue (202, 203, 208)	7/7.1	98
Total	Person-years 37,425 No. of employees 5,297 No. of deaths 1,180	

^a Expected (Exp) deaths based on age, sex, race, and cause-specific U.S. population rates calculated for each five year calendar period. Obs is observed deaths.

^b The SMR is statistically significant at $p < 0.05$, if confidence interval (CI) does not include 100.

^c International Classification of Diseases, eighth revision codes shown in brackets.

^d The SMRs were not calculated for sites with only one observed death; these were: larynx, small intestine, peritoneum, testis, and Hodgkin's disease; three observed deaths from myeloid leukemia (ICD-9 205), included in the total lymphatic category, are not shown separately.

Table 9—Standardized Mortality Ratios (SMRs) for Deaths by Cancer Site and by Occupational Category Among Employees World-Wide, 1950-1977 Cohort

Cancer Site	Occupational Category*			All Other
	Operator, Mechanic, and Laborer	SMR (%)	95% CI	
All malignant neoplasms (148-208)†	264/287.4	98	95-112	91.07
Esophagus (148-149)	215.8	34	4-123	...
All digestive organs (150-159)	61.54.2	105	89-126	...
Stomach (150)	718.9	117	47-261	...
Small intestine (151)	19/19.8	92	44-189	...
Large intestine (152)	24/19.1	105	64-162	...
Rectum (154)	216.9	33	4-118	...
Liver, gallbladder, bile duct (155, 156)	327.4	59	19-237	...
Pancreas (157)	10/11.7	194	81-548	...
Empyretic system (160-163)	67/69.2	96	81-113	...
Lung (162)	86/95.8	91	71-112	...
Bladder (164)	172.9	33	4-154	...
Bladder (165)	24/28.4	96	58-158	...
Prostate (166)	18/23.4	96	58-158	...
Bladder (167)	87/7.8	114	49-274	...
Bladder (168)	94.9	299	19-525	...
Bladder/CNS (181-182)	323.4	96	82-118	...
Brain, connective tissue, skin breast (179-174)	21/14.8	104	72-150	...
Other, secondary and unspecified sites (179-180)	21/12.9	124	72-180	...
All lymphoproliferative (200-208)	121.1	124	72-180	...
Lymphoproliferative (200-208)	121.1	124	72-180	...
Leukemia (204-207)	775.8	125	69-214	...
Other lymphoproliferative (202, 203, 206)	21/42.3	...	...	...
Total	...	...	...	...
	Person years	21,423.3	9,543.1	...
	No. of employees	2,818	1,316	...
	No. of deaths	216	116	...
	No. of cancer deaths	204	48	...

* Excludes 83 workers with missing work histories; of these, 29 were incident cases (cancer deaths).

† Expected (Exp) numbers of deaths based on age, sex, race, and cause-specific U.S. population rates calculated for each five-year period; this is observed deaths.

‡ The SMR is statistically significant at $p < 0.05$ if confidence interval (CI) does not include 100.

§ International Classification of Diseases (ICD-9) code for neoplasms (140-208).

|| The SMRs were not calculated for sites with only one observed death; these sites: larynx, nasopharynx, testis, and Hodgkin's disease.

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AND CHEMICAL PLANT WORKERS

Table 10—Excess Range Refinery and Chemical Plant (1978-1977) Pancreatic Cancer Analysis by Occupation and by Smoking History (N=24)

Case	Occupational Category	Sex*	H Ever Smoked	Smoking History		Age at Death, (years)
				Type	Quantity/Smoked (Packs/Day)	
1	Mechanic	M/W	Yes	1	0.5-1	65.8
2	Technician	M/W	Yes	1	1-2	67.2
3	Mechanic	M/W	Yes	1	0.5-1	75.1
4	Laborer	M/W	Yes	1	0.5-1	71.4
5	Technician	M/W	Unknown	...	...	62.8
6	Operator	M/W	No	...	...	70.2
7	Mechanic	M/W	Yes	1	0.5-1	61.8
8	Manager	M/W	Yes	1	0.5-1	68.9
9	Mechanic	M/W	Yes	2	...	74.3
10	Mechanic	M/W	Unknown	...	...	82.6
11	Mechanic	M/W	No	...	...	71.9
12	Mechanic	M/W	Yes	1	0.5-1	73.6
13	Laborer	M/W	Yes	1.2	...	69.4
14	Mechanic	M/W	Unknown	...	...	85.7
15	Mechanic	M/W	Yes	2	...	76.6
16	Laborer	M/W	Yes	1.2, 2.3	<0.5	71.2
17	Mechanic	M/W	Yes	1	<0.5	83.7
18	Mechanic	M/W	Unknown	...	...	85.1
19	Office	F/W	Yes	1	0.5-1	74.7
20	Mechanic	M/W	Yes	1	0.5-1	63.6
21	Mechanic	M/W	No	...	...	67.2
22	Manager	M/W	Yes	...	...	69.9
23	Mechanic	M/W	Yes	1	0.5-1	59.8
24	Mechanic	M/W	Yes	1	0.5-1	71.2

* Sex: M indicates male; F, female; RW, female; RW, nonwhite.

† Tobacco type: 1, cigarettes; 2, cigars; 3, chewing tobacco.

‡ For cigarette smokers only.

involving exposures to petroleum and petrochemicals, 11.2 we examined our data for cancer of the pancreas in particular detail.

A case-analysis of the 24 known cases of cancer of the pancreas was performed to examine distributions by occupational categories, cigarette-smoking histories, and alcohol-consumption patterns. Since the majority of decedents had "unknown" alcohol-consumption patterns, analyses with this variable were impossible. Distributions by occupational category, and by sex, race, smoking histories, and age at death are given in Table 9. The average age at death of the decedents with pancreatic cancer was 71.8 years. Fifty-eight percent of the decedents worked mainly as mechanics throughout their careers in the Baton Rouge plant. The percentage of mechanics (60%) in the total work-force population was similar.

The SMRs for cancer of the pancreas for the occupational grouping of process operators, mechanics, and laborers and for all other occupations combined were 154 and 156, respectively. Similar

petroleum refining and petrochemical workers. Although deaths due to cancer of the pancreas, testis, kidney, and brain/CNS and deaths due to lymphoreticular sarcoma were higher than expected in this cohort, the differences were ones that might easily have occurred by chance. The only cancer of the digestive system that was of borderline significance in the present study was cancer of the pancreas.

If the one probable pancreatic cancer case that had to be excluded for nosological reasons could have been justifiably included in the observed deaths, an SMR of 159 (95% confidence interval of 102 to 237) would have resulted. Cancer of the pancreas is a major contributor to malignant neoplastic deaths in the U.S. population, particularly in Louisiana, and is reported to be increasing rapidly.^{21,22} Since cancer of the pancreas has been associated with occupations

results were observed for those hired before 1956. Since neither excess was dramatically high nor statistically significant, the occupational category did not offer an obvious explanation for the elevated overall SMR for cancer of the pancreas. This result is contrary to that expected on the basis of the Lin-Kessler study²³ that showed an association with occupations involving exposure to gasoline. Unfortunately, no data were available to address the issues of a common exposure (other than the crude breakdown by occupation) or of dietary or socioeconomic factors.

Blot et al.²¹ in examining U.S. age-adjusted pancreatic cancer mortality rates by county for the period 1950 to 1969, identified a geographic clustering of deaths in the southern Acadian parishes in Louisiana, as well as in some northern parishes extending into the state of Mississippi. Noting the strong correlation of pancreatic cancer with lung cancer, these investigators suggested that tobacco consumption might be a factor in the development of cancer of the pancreas. However, no excess of lung cancer was found in this study. Smoking was one of the covariates considered for analysis. The available smoking data were abstracted from the medical records and summarized, but since many smoking histories were unknown, we are unable to offer any comment about this factor.

A recently reported study²² was undertaken to determine if the association observed in Louisiana on the county/parish aggregate level by Blot et al also existed when a case-control study was done. A comparison of 399 white men who died of pancreatic cancer with matched controls who did not die of cancer revealed a twofold but not statistically significant increase in pancreatic mortality among those who had worked for oil-refining and paper-manufacturing industries. In addition, the odds ratio was slightly increased among white men of "probable" and "possible" Acadian ancestry.

Since the southern Acadian parishes of Louisiana were pinpointed as counties with high pancreatic cancer mortality, it is possible that some factors indigenous to the area may be acting on this occupational population as well. Blot et al have noted an association of pancreatic cancer with persons of Scandinavian and Eastern European descent. Ethnic association could not be examined in our study because ethnicity data were not available for our population.

Another recent study of 369 cases and 644 controls found a strong association between coffee consumption and pancreatic cancer.²⁴ Additional investigations are required to examine this complex, and probably multifactorial, association.

It is possible that dilution effects from persons in the population with less than 15 years of employment may be masking potential associations. To rule out such a dilution effect, we examined the mortality experience for those with 15 or more years of employment at the Baton Rouge site. The results were similar to those observed for the total cohort. Minor fluctuations were observed in the "all other" occupational category as follows: the SMR for cancer of the pancreas changed from 156 to 161; that for bone, connective tissue, skin, and breast increased from 150 to 176; and the SMR for lymphoreticular sarcoma increased from 100 to 333. This variability could be attributed to the decrease in the denominator population and to the low number of deaths.

It is possible that statistically significant differences were missed because of the relatively small numbers of deaths, particularly in the stratified analyses, but it is highly unlikely that a real relative risk difference of twofold to threefold would have been missed with a population of this size had there been a strong association between cancer mortality and employment at our Baton Rouge refinery and chemical plants.

Summary

The 1970 to 1977 mortality experience of petroleum refinery and petrochemical workers at Exxon's Baton Rouge refinery and chemical plant was examined in a retrospective cohort analysis. In general, both total mortality and overall cancer mortality were lower among the employee population than among the U.S. population of similar age, sex, and race. The SMRs for cancer of the kidney, testis, pancreas, brain/CNS, and SMRs of lymphoproliferative cancers were above 100 in the study population, but these elevations were not statistically significant. The only observation of borderline significance was in the category of pancreatic cancer. Although deaths due to cancers of certain sites occurred more often than expected among workers presumed to be exposed (i.e., operators, mechanics, and laborers), the number of overall cancer deaths was slightly less than expected on the basis of the U.S. population. Exclusion of employees with less than 15 years of experience did not alter the results or interpretations.

Some similarities to the results of other petroleum studies were observed, but these have not been consistent across all such studies. As in any hypothesis-generating study, these results suggest areas for further investigation.

References

1. Baird, V.C.: Effects of atmospheric contamination on cancer mortality in petroleum refinery employees. *JOM* 9:415-420, 1967.
2. Baylor, C.H., Weaver, N.K.: A health survey of petroleum asphalt workers. *Med. Bull. Stand. Oil Co.* 29:5-12, 1969.
3. Benini, F.: Occupational diseases due to hydrocarbons observed in the workers of an oil refinery. *La Medicina Del Lavoro* 47:153-161, 1956.
4. Eckardt, R.E.: Carcinogenicity of petroleum products (with particular reference to the automotive industry). *Ind. Med. Surg.* 26:396-398, 1957.
5. Wade, L.: Observations on skin cancer among refinery workers. Limited to men exposed to high-boiling fractions. *Arch. Environ. Health* 6:730-735, 1963.
6. Cole, P., Hoover R., Friedell G.H.: Occupation and cancer of the lower urinary tract. *Cancer* 29:1250-1260, 1972.
7. Cole, P., Monson, R.R., Haning, H., et al: Smoking and cancer of the lower urinary tract. *N. Engl. J. Med.* 284:129-134, 1974.
8. Menck, H.R., Henderson, B.E.: Occupational differences in rates of lung cancer. *JOM* 18:797-801, 1976.
9. Howe, G.R., Burch, J.D., Miller, A.B., et al: Tobacco use, occupation, coffee, various nutrients, and bladder cancer. *J. Natl. Cancer Inst.* 64:701-713, 1980.
10. Gaffey, W., Weaver, N.K., Tabershaw, I.P.A.: Mortality Study of Petroleum Refinery Workers. Washington, D.C.: The American Petroleum Institute, 1974.
11. Thomas, T.L., Deconfle, P., Moure-Eraso, R.: Mortality among workers employed in petroleum refining and petrochemical plants. *JOM* 22:97-103, 1980.
12. Theriault, G., Goulet, L.: A mortality study of oil refinery workers. *JOM* 21:367-370, 1979.
13. Hanis, N.M., Stavratsky, K.M., Fowler, J.L.: Cancer mortality in oil refinery workers. *JOM* 21:167-174, 1979.
14. World Health Organization: Manual of the International Classification of Diseases, Injuries, and Causes of Death. eighth revision. Geneva: WHO, 1967.

15. Barr, A.J., Goodnight, J.H., Sall, J.P., et al: A User's Guide to SAS-76. Raleigh, N.C., SAS Institute Inc., 1976.
16. Monson, R.R.: Analysis of relative survival and proportional mortality. *Comput. Biomed. Res.* 7:325-332, 1974.
17. Bailar, J.C., Ederer, F.: Significance factors for the ratio of a Poisson variable to its expectation. *Biometrics* 20:639-642, 1964.
18. Colton, T.: Statistics in Medicine. Boston: Little Brown & Co., 1974.
19. Fox, A.J., Collier, P.F.: Low mortality rates in industrial cohort studies due to selection for work and survival in the industry. *Br. J. Prev. Soc. Med.* 30:225-230, 1976.
20. McMichael, A.J.: Standardized mortality ratios and the "Healthy Worker Effect." *JOM* 18:164-168, 1976.
21. Blot, W.J., Fraumeni, F.J. Jr., Storie, B.J.: Geographic correlates of pancreatic cancer in the United States. *Cancer* 42:373-380, 1978.
22. Pickle, L.W., Gottleib, M.S.: Pancreatic cancer mortality in Louisiana. *Am J Public Health* 70:256-259, 1980.
23. Lin, R.S., Kessler I.I.: A multifactorial model for pancreatic cancer in man. *JAMA* 245:147-152, 1981.
24. MacMahon, B., Yen, S., Trichopoulos, D., et al: Coffee and cancer of the pancreas. *N. Engl. J. Med.* 34:630-700, 1981.