Exhibit 316

A 56-Year Mortality Follow-Up of Texas Petroleum Refinery and Chemical Employees, 1948–2003

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Objective: *To further investigate the mortality risk of employees who worked in the petroleum refinery industry, we updated an earlier investigation by extending the mortality follow-up by an additional 14 years through 2003.* ***Methods:*** *The cohort consisted of 10,621 employees with an average follow-up of 34 years. We used the standardized mortality ratio (SMR) adjusted for age, race, and calendar years as a measure of risk.* ***Results:*** *Overall mortality (SMR = 0.77, 95% confidence interval [CI], 0.74–0.79), all cancer mortality (SMR = 0.87, 95% CI = 0.82–0.93), and most cause-specific mortalities for the total study population were lower than or similar to that of the population of Harris County, Texas. This study did not show a significant increase in leukemia in the total population or in any of the subgroups. The only statistically significant excess of mortality found in this study was an increase in mesothelioma among maintenance employees; the SMR was 4.78 (95% CI = 2.54–8.17) among employees who worked for a minimum of one year and was 7.51 (95% CI = 3.75–13.45) among those with 10 or more years of employment and 20 or more years of latency.* ***Conclusions:*** *After more than half a century of follow-up, employees at this facility continue to show more favorable mortality outcomes than the general local population. Overall, no statistically significant increase of leukemia or of any of the specific cell types was found. The increased mesothelioma is likely related to past exposure to asbestos.* (J Occup Environ Med. *2007;49:557–567*)

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The Deer Park refinery began operations in 1929 with approximately 500 employees. The addition of a new chemical division in 1941 incorporated another 55 employees, including many transfers from the refinery. Through the mid 1940s and the early 1950s, operations significantly expanded and the last 60 years have seen numerous changes, including the addition of new units, as well as the shutdown or selling of other units, and process changes at both the refinery and chemical plant.

Today, the Shell Deer Park Manufacturing Complex (DPMC) refines crude oil and manufactures various fuels and petrochemicals such as benzene, toluene, isopropyl alcohol, and butadiene. Other potentially hazardous substances found at the facility include hydrogen sulfide, polynuclear aromatics, asbestos, and various solvents. In the past, manufacturing also included epichlorohydrin, epoxy resins, vinyl chloride, oil lubricants, and other products. Patterns of potential chemical exposure have likely changed over the years with the changes in equipment technologies and in work practices. The complex is currently one of the larger oil refinery/petrochemical plants in the United States, employing approximately 1750 workers.

Since the late 1970s, a large number of epidemiological studies of petroleum workers have been conducted to examine the possible adverse health effects of employment in facilities where workers are potentially exposed to a variety of refinery

products and chemical agents, including benzene and other hydrocarbons.[1–17] In a previous report, the mortality of employees from the DPMC was followed up through 1989.[7] Results from these analyses were generally favorable in that the all-cause mortality, overall cancer mortality, and deaths from most specific causes were lower than those of the comparable local population in Harris County, Texas, where the facility is located. However, mortality from certain diseases including mesothelioma and cancer of lymphopoietic tissue was increased, particularly among long-term employees.

The purpose of this study was to update the earlier study by extending the mortality follow-up through 2003. Employees who were hired or transferred to the DPMC since 1990 have also been included. A total of 10,621 employees were included in this update. The large size of this cohort and the additional 14 years of follow-up provide substantially increased statistical power to the previous cohort in quantifying any mortality risks associated with having worked at this facility.

Materials and Methods

The previous study consisted of 9720 subjects, which included all male and female hourly production and maintenance employees, as well as all salaried employees with routine field or laboratory assignments, employed at least 3 cumulative months at the DPMC from January 1, 1948, to December 31, 1989. Salaried employees included foremen, first-line supervisors, chemists, laboratory technicians and certain engineering, quality control, and security personnel. Analysis of hourly and salaried employees separately was not feasible because some employees, such as foremen and first-line supervisors, may have progressed from hourly to salaried during their employment at this facility and simply presenting the results as "ever/never hourly" would not add much in the way of detail. A detailed description of the study cohort was reported elsewhere.[7] For this update, the population consisted of employees who had worked at the DPMC for at least 3 months from 1948 to 2003 and who met the previous study eligibility criteria. A total of 10,621 employees were identified.

Source documents for the study include work history and personnel records retrieved from the plant for the period between 1948 and 1976 and computerized records from Shell's human resources system, containing demographic and work history records for all employees from 1973 on. Cohort members' work histories were brought up to date through 2003 and were coded with an updated version of the original study's coding manual. A more detailed description is provided elsewhere.[7]

Vital status as of December 31, 2003, for each study member was determined from a number of sources, including company records, the Social Security Administration's (SSA's) Master Beneficiary file, and the National Death Index (NDI), which has been shown to have almost complete ascertainment of deaths (97%) occurring since 1979.[18,19] A total of 1641 cohort employees were actively employed at DPMC as of December 31, 2003, and were classified as living. Persons who were presumed living as of December 31, 1989, the end of the previous study, were also presumed living as of December 31, 2003, if no death record was found from the vital status sources. Forty-five deaths were identified among employees with unknown vital status at the end of the previous study ($n = 136$), and no death records were found for the remaining 91 employees who were classified as lost to follow-up in this update. Those employees who were terminated after December 31, 1989, and who were not identified by SSA or NDI searches were assumed to be alive.

Death certificates were obtained for deceased employees, when available, from company benefit files. Death certificates for those potential decedents identified by the SSA, NDI, or both were requested from the respective state vital statistics departments and verified with company information to ensure a correct match between these records. A certified nosologist trained by the National Center for Health Statistics, according to rules of the International Classification of Diseases (ICD) in effect at the time of death, coded the underlying cause of death.

An employee entered the follow-up period on April 1, 1948, if he or she began employment before 1948. Otherwise, he or she entered the study 3 months after the start of employment at DPMC. Person-years were accumulated from the entry date until the earliest of either the date of death, the study end date (December 31, 2003), or the date of lost to follow-up.

The mortality experience for selected causes is expressed as a standardized mortality ratio (SMR). SMRs and corresponding 95% confidence intervals were calculated with the Occupational Cohort Mortality Analysis Program (OCMAP), using the ICD revision in effect at the time of death.[20] The SMR is the number of observed deaths in the study group divided by the number of deaths that would be expected if the study group experienced the same death rates as a comparison population. The number of expected deaths was adjusted for age, race, and time period. Employees with unknown race ($n = 2892$) were included as white for statistical analyses. In addition, to help control for geographic variations in mortality, we used death rates for Harris County, Texas, where the majority of the study population resides, as the comparison. We performed statistical analyses on the total cohort, subcohorts stratified by primary work location (ie, refinery or chemical plant), calendar year of hire, and length of employment.

County mortality rates were obtained from the Mortality and Population Data System (MPDS), which includes cancer death rates starting from 1950.[21] For the period between 1948 and 1949, expected deaths from cancer were calculated based on rates between 1950 and 1954. Noncancer MPDS mortality rates begin in 1962, so rates between 1962 and 1964 were applied to calculate expected deaths for 1948 to 1959. A total of 60 deaths for which no death certificate was obtained were included in the overall analyses, but not in the specific cause analyses.

Because of the potential for benzene exposure in the refinery environment and the a priori interest in benzene-associated leukemia,[17,22–24] a cell-type specific analysis was conducted for acute non-lymphocytic leukemia (ANLL), acute lymphocytic leukemia (ALL), chronic lymphocytic leukemia (CLL), acute myelocytic leukemia (AML), and chronic myelocytic leukemia (CML). Because of the relatively small number of deaths in Harris County, national death rates for these cell types were used to calculate the expected numbers of deaths from cell-type specific leukemia. Age-specific leukemia cell-type mortality rates from 1969 to 1977[25] were used to calculate the expected number of deaths before 1980. Similar data from 1982 through 1986, published by the National Cancer Institute, were used to calculate the expected numbers for 1980 to 1989.[26] Mortality rates from 1990 to 2003, retrieved from the National Cancer Institute database, were applied to the corresponding years of the study population. The ICD codes (according to the 9th revision codes) for ALL, CLL, and CML were 204.0, 204.1, and 205.1, respectively. Three ICD codes were used to identify AML: 205.0, 207.0, and 207.2. Acute non-lymphocytic leukemia was limited to the two main subtypes: AML and acute monocytic leukemia (ICD code 206.0).

To further evaluate any excess mesothelioma deaths in this facility and to assess other potential asbestos-related cancer risks among employees with the greatest potential for asbestos exposure, we examined a subgroup of male employees who had worked in maintenance jobs for a minimum of 1 year (n = 2569). The jobs included insulators, pipefitters, boilermakers, electricians, welders, carpenters, and laborers. Because long latent periods are usually required for chronic diseases to develop, a subgroup of male employees who had worked for 10 or more years in maintenance jobs, with 20 or more years since their first potentially exposed job (n = 1222), was also examined.

Results

The 10,621 study cohort members contributed 353,724 person-years during the 56-year observation period. This updates the previous cohort by 107,503 person-years. Male employees were followed an average of 34 years, whereas the average follow-up for female employees was 25 years. More than half of male employees (54%) were hired before 1960, whereas the majority of female employees (86%) started working at this facility after 1970. The average duration of employment for men was 17 years and for women,11 years.

Male employees comprised almost 92% of the cohort (Table 1). The majority of male employees in the cohort were either retired (34.3%) or terminated (47.3%). Of all male employees included in the cohort, 64% were alive and 35% were deceased. Death certificates were obtained for more than 98% of the identified deaths.

Overall mortality was significantly lower for male employees at the refinery (SMR = 0.80, 95% CI = 0.77–0.84), chemical plant (SMR = 0.71, 95% CI = 0.67–0.75), and the total cohort (SMR = 0.77, 95% CI = 0.74–0.79) compared to that of the general population in Harris County, Texas (Table 2). Contributing to the deficit in overall mortality was the significant decrease in mortality from a number of chronic diseases such as diabetes mellitus (SMR = 0.58, 95% CI = 0.43–0.75), cerebrovascular disease (SMR = 0.67, 95% CI = 0.57–0.78), heart disease (SMR = 0.73, 95% CI = 0.69–0.77), non-malignant respiratory disease (SMR = 0.82, 95% CI = 0.72–0.93), and liver cirrhosis (SMR = 0.47, 95% CI = 0.35–0.62). Similar patterns were seen for the refinery and chemical plant populations.

Mortality from all malignant neoplasms was significantly decreased in the total population (SMR = 0.87, 95% CI = 0.82–0.93), as well as in the refinery (SMR = 0.87, 95% CI = 0.81–0.95) and chemical (SMR = 0.87, 95% CI = 0.79–0.97) populations (Table 2). Mortality

TABLE 1
Distribution of Study Population by Vital Status as of January 1, 2004

	Male		Female		Total	
Employment and Vital Status	N	%	N	%	N	%
Currently employed	1482	15.2	159	18.6	1641	15.5
Terminated	4620	47.3	534	62.3	5154	48.5
Alive	3122	(67.6)	501	(93.8)	3623	(70.3)
Dead	1413	(30.6)	27	(5.1)	1440	(27.9)
Unknown status	85	(1.8)	6	(1.1)	91	(1.8)
Retired	3345	34.3	159	18.6	3504	33.3
Alive	1637	(48.9)	130	(81.8)	1767	(50.4)
Dead	1708	(51.1)	29	(18.2)	1737	(49.6)
Unknown status	0	(0)	0	(0)	0	(0)
Died while employed	317	3.2	5	0.6	322	3.0
TOTAL	9764	100	857	100	10,621	100

Values in parentheses represent the percentage of the corresponding subcategory.

TABLE 2
Observed Deaths and Standardized Mortality Ratios (SMRs)[a] of Male Employees, 1948–2003

	Refinery (n = 5468; 184,042.6 person-yrs)			Chemical (n = 4296; 148,485.6 person-yrs)			Total (n = 9764; 332,527.9 person-yrs)		
Cause of Death (8th ICD revision code)	**Observed**	**SMR**	**95% CI**	**Observed**	**SMR**	**95% CI**	**Observed**	**SMR**	**95% CI**
All causes (001–999)	2204	0.80*	0.77–0.84	1234	0.71*	0.67–0.75	3438	0.77*	0.74–0.79
All malignant neoplasms (140–209)	590	0.87*	0.81–0.95	391	0.87*	0.79–0.97	981	0.87*	0.82–0.93
Buccal cavity, pharynx (140–149)	12	0.69	0.35–1.20	9	0.80	0.36–1.51	21	0.73	0.45–1.11
Digestive organs, peritoneum (150–159)	145	0.91	0.77–1.07	85	0.83	0.66–1.02	230	0.88*	0.77–1.00
Esophagus (150)	17	0.94	0.55–1.51	10	0.82	0.39–1.51	27	0.89	0.59–1.30
Stomach (151)	18	0.84	0.50–1.32	7	0.56	0.23–1.56	25	0.74	0.48–1.09
Large intestine (153)	54	1.01	0.76–1.31	34	0.97	0.67–1.35	88	0.99	0.80–1.22
Rectum (154)	14	1.31	0.72–2.20	2	0.29	0.03–1.03	16	0.90	0.52–1.47
Biliary passages, liver primary (155,156)	14	0.70	0.38–1.17	11	0.81	0.40–1.45	25	0.74	0.48–1.10
Pancreas (157)	26	0.81	0.53–1.19	20	0.98	0.60–1.52	46	0.88	0.64–1.17
Respiratory system (160–163)	211	0.80*	0.70–0.92	150	0.85*	0.72–0.99	361	0.82*	0.74–0.91
Bronchus, trachea, lung (162)	201	0.80*	0.69–0.92	145	0.85	0.72–1.00	346	0.82*	0.74–0.91
Prostate (185)	61	0.96	0.73–1.23	32	0.86	0.59–1.21	93	0.92	0.74–1.13
Kidney (189.0,189.2)	14	0.84	0.46–1.42	7	0.60	0.24–1.24	21	0.74	0.46–1.14
Bladder and other urinary organs (188,189.9)	14	0.86	0.47–1.45	6	0.62	0.23–1.36	20	0.77	0.47–1.20
Malignant melanoma of skin (172)	5	0.48	0.15–1.11	7	0.86	0.34–1.76	12	0.64	0.33–1.12
Central nervous system (191,192)	13	0.77	0.41–1.32	14	1.12	0.61–1.87	27	0.92	0.61–1.34
All lymphatic, hematopoietic tissue (200–209)	62	0.98	0.75–1.25	41	0.94	0.67–1.27	103	0.96	0.79–1.17
Hodgkin disease (201)	4	1.16	0.32–2.97	0	–	0.0–1.63	4	0.70	0.19–1.79
Non-Hodgkin lymphoma (200,202)	27	1.13	0.74–1.64	13	0.75	0.40–1.28	40	0.97	0.69–1.32
Leukemia, aleukemia (204–207)	23	0.95	0.60–1.42	18	1.10	0.65–1.73	41	1.01	0.72–1.36
Diabetes mellitus (250)	36	0.66*	0.46–0.92	17	0.45*	0.26–0.72	53	0.58*	0.43–0.75
Cerebrovascular disease (430–438)	110	0.68*	0.56–0.82	56	0.65*	0.49–0.84	166	0.67*	0.57–0.78
All heart disease (390–398,400.1,400.9, 402,404,410–414,420–429)	767	0.78*	0.72–0.83	380	0.64*	0.58–0.71	1147	0.73*	0.69–0.77
Nonmalignant respiratory disease (460–519)	171	0.85*	0.73–0.99	91	0.77*	0.62–0.94	262	0.82*	0.72–0.93
Cirrhosis of liver (571)	28	0.44*	0.29–0.64	23	0.51*	0.32–0.76	51	0.47*	0.35–0.62
Accidents (E800–E949)	117	0.89	0.73–1.06	66	0.68*	0.52–0.86	183	0.80*	0.69–0.93
Suicide (E950–E959)	45	0.81	0.59–1.08	27	0.63*	0.41–0.92	72	0.73*	0.57–0.92
Homicides, other external causes (residual)	20	0.39*	0.24–0.60	11	0.26*	0.13–0.47	31	0.33*	0.22–0.47
Unknown causes of death	45	–	–	15	–	–	60	–	–

*$P < 0.05$.
[a]Expected number of deaths based on the Harris County (Texas) male population, ICD revision in effect at the time of death.

from several specific cancer sites was also decreased including cancers of the digestive organs and peritoneum (SMR = 0.88, 95% CI = 0.77–1.00) and lung cancer (SMR = 0.82, 95% CI = 0.74–0.91). There was no significant increase for any specific cancer site in any of the groups. However, cancer of the rectum showed a non-significant increase among refinery employees (SMR = 1.31, 95% CI = 0.72–2.20). There were also slight increases in mortality from Hodgkin disease (SMR = 1.16, 95% CI = 0.32–2.97) and non-Hodgkin lymphoma (SMR = 1.13, 95% CI = 0.74–1.64) among refinery employees, and from leukemia (SMR = 1.10, 95% CI = 0.65–1.73) and cancer of the central nervous system (SMR = 1.12, 95% CI = 0.61–1.87) among the chemical plant employees, but none of these was significant.

The use of national rates as a comparison population generally decreased the number of expected deaths by 3% to 5%. Mortality from all causes (SMR = 0.80, 95% CI = 0.77–0.83), all cancers (SMR = 0.91, 95% CI = 0.86–0.97), and heart disease (SMR = 0.75, 95% CI = 0.70–0.79), for example, was lower than expected. Mortality from leukemia was similar to the national experience (SMR = 1.04, 95% CI = 0.75–1.41). Mortality from lung cancer was also similar to national rates (SMR = 0.92, 95% CI = 0.83–1.02). However, the SMR was 12% greater than the SMR calculated using Harris County as the comparison population, reflecting a generally higher mortality in the county for this cancer during the study period. Interestingly, mortality from non-malignant respiratory disease in the study population was lower compared with Harris County (SMR = 0.76, 95% CI = 0.67–0.85) than compared with the general US population (SMR =

TABLE 3
Mortality From Cancers of the Digestive and Respiratory Systems and Mesothelioma Among Maintenance Employees With Potential Exposure to Asbestos, 1948–2003

	Total[a] (n = 2569)				≥20 yrs Latency[b] (n = 1222)			
Cause of Death (8th ICD revision code)	Observed	Expected[d]	SMR	95% CI	Observed	Expected[c]	SMR	95% CI
All causes (001–999)	1261	1487.56	0.85*	0.80–0.90	695	825.39	0.84*	0.78–0.91
All malignant neoplasms (140–209)	353	390.35	0.90	0.81–1.00	193	208.45	0.93	0.80–1.07
Buccal cavity, pharynx (140–149)	6	10.10	0.59	0.22–1.29	2	5.09	0.39	0.05–1.42
Digestive organs, peritoneum (150–159)	84	94.53	0.89	0.71–1.10	48	50.48	0.95	0.70–1.26
Esophagus (150)	9	11.26	0.80	0.37–1.52	3	5.78	0.52	0.11–1.52
Stomach (151)	10	13.63	0.73	0.35–1.35	4	7.14	0.56	0.15–1.43
Large intestine (153)	27	31.02	0.87	0.57–1.27	18	17.23	1.04	0.62–1.65
Rectum (154)	6	6.16	0.98	0.36–2.12	3	3.18	0.94	0.19–2.75
Biliary passages, liver primary (155,156)	10	11.64	0.86	0.41–1.58	7	6.10	1.15	0.46–2.36
Pancreas (157)	20	18.50	1.08	0.66–1.67	11	9.99	1.10	0.55–1.97
Respiratory system (160–163)	137	150.85	0.90	0.76–1.07	66	80.01	0.83	0.64–1.05
Larynx (161)	4	4.89	0.82	0.22–2.10	3	2.56	1.17	0.24–3.42
Bronchus, trachea, lung (162)	130	144.53	0.90	0.75–1.07	63	76.73	0.82	0.63–1.05
Mesothelioma[d]	13	2.72	4.78*	2.54–8.17	11	1.46	7.51*	3.75–13.45

*P< 0.05.
[a]Employees who had worked ≥1 yr in a maintenance job (91,876.5 person-yrs).
[b]Employees who worked for ≥10 yrs in a maintenance job and had ≥ 20 yrs of latency (25,792.5 person-yrs).
[c]Expected number of deaths based on the Harris County (Texas) male population, ICD revision in effect at the time of death.
[d]Expected number of deaths based on SEER US incidence rates, 1973–2003.

0.82, 95% CI = 0.72–0.93). The data is not shown.

Because of the use of asbestos containing materials as insulation at the complex in the past, we also examined mortality from mesothelioma, which has been associated with asbestos exposure. For deaths from mesothelioma, routine ICD coding was not used but rather all death certificates were reviewed for any mention of mesothelioma. The review revealed 21 deaths with mesothelioma mentioned among male employees. Incidence rates for 1973 to 2003 from the Surveillance, Epidemiology, and End-Results (SEER) Program were used to estimate the expected number of deaths because age-specific mortality rates were not available for the Harris County population. For the total male cohort, 8.40 deaths from mesothelioma would have been expected, resulting in a statistically significant SMR of 2.50 (95% CI = 1.55–3.83). Fourteen of the 21 cases were identified during the follow-up from 1990 to 2003. The SMR during the 14-year update period was 2.63 (95% CI = 1.44–4.42), which was higher than that reported in the previous study.

Table 3 presents the observed and expected deaths, SMR, and 95% confidence limits for potentially exposed maintenance employees for selected cancer sites. Among employees who had worked at least 1 year in maintenance jobs, the overall mortality was 15% lower (SMR = 0.85, 95% CI = 0.80–0.90), and cancer mortality was 10% lower (SMR = 0.90, 95% CI = 0.81–1.00), than comparable rates in Harris County. Generally, there was no increase in mortality from any specific cancer sites. However, based on 13 observed and 2.72 expected deaths, mortality from mesothelioma was significantly increased (SMR = 4.78, 95% CI = 2.54–8.17). Among employees who worked for 10 or more years in maintenance jobs and also had 20 or more years of latency, overall mortality (SMR = 0.84, 95% CI = 0.78–0.91) and all cancer mortality (SMR = 0.93, 95% CI = 0.80–1.07) was also decreased. However, based on 11 expected and 1.46 observed deaths, mortality from mesothelioma was increased in this group (SMR = 7.51, 95% CI = 3.75–13.45).

Table 4 shows the patterns of mortality for male employees by calendar year of first employment: before 1950, 1950 to 1959, and after 1960. Overall mortality was significantly lower than that in the corresponding Harris County population for all three-time periods of hire, with SMRs of 0.85 (95% CI = 0.82–0.88), 0.66 (95% CI = 0.61–0.71), and 0.57 (95% CI = 0.51–0.64), respectively. A similar pattern was noted for all malignant neoplasms, with SMRs of 0.94 (95% CI = 0.87–1.01) among employees hired before 1950, 0.79 (95% CI = 0.70–0.90) between 1950 and 1960, and 0.72 (95% CI = 0.57–0.89) among the most recent hires. However, nonsignificant increases in mortality from non-Hodgkin lymphoma were seen among employees in the earliest hire group (SMR = 1.12, 95% CI = 0.73–1.64). Among employees hired after 1960, mortality from cancer of the large intestine was increased, albeit not significantly (SMR = 1.62,

TABLE 4
Observed Deaths and Standardized Mortality Ratios (SMRs)[a] of Male Employees by Period of Hire, 1948–2003

	Before 1950 (n = 3230; 131,824.2 person-yrs)			1950–1959 (n = 2067; 90,161.4 person-yrs)			After 1960 (n = 4467; 110,542.8 person-yrs)		
Cause of Death (8th ICD revision code)	**Observed**	**SMR**	**95% CI**	**Observed**	**SMR**	**95% CI**	**Observed**	**SMR**	**95% CI**
All causes (001–999)	2399	0.85*	0.82–0.88	722	0.66*	0.61–0.71	317	0.57*	0.51–0.64
All malignant neoplasms (140–209)	651	0.94	0.87–1.01	248	0.79*	0.70–0.90	82	0.72*	0.57–0.89
Buccal cavity, pharynx (140–149)	19	1.09	0.65–1.70	1	0.13*	0.00–0.72	1	0.28	0.01–1.56
Digestive organs, peritoneum (150–159)	155	0.95	0.81–1.11	47	0.66*	0.79–0.88	28	1.00	0.66–1.44
Esophagus (150)	16	0.91	0.52–1.48	7	0.76	0.31–1.57	4	1.13	0.31–2.90
Stomach (151)	17	0.75	0.44–1.21	6	0.75	0.27–1.62	2	0.59	0.07–2.13
Large intestine (153)	57	1.02	0.77–1.32	17	0.71	0.41–1.13	14	1.62	0.88–2.71
Rectum (154)	11	1.03	0.52–1.85	5	0.99	0.32–2.32	0	—	0.00–1.82
Biliary passages, liver primary (155,156)	18	0.92	0.54–1.45	5	0.53	0.17–1.23	2	0.44	0.05–1.60
Pancreas (157)	34	1.03	0.71–1.43	6	0.44*	0.16–0.95	6	1.12	0.41–2.43
Respiratory system (160–163)	231	0.86*	0.75–0.98	107	0.83	0.68–1.00	23	0.56*	0.35–0.84
Bronchus, trachea, lung (162)	218	0.85*	0.74–0.97	105	0.85	0.69–1.02	22	0.56*	0.35–0.85
Prostate (185)	72	0.98	0.76–1.23	18	0.78	0.46–1.23	3	0.76	0.16–2.22
Kidney (189.0,189.2)	13	0.79	0.42–1.35	6	0.72	0.27–1.57	2	0.58	0.07–2.11
Bladder and other urinary organs (188,189.9)	15	0.82	0.46–1.36	3	0.50	0.10–1.45	2	1.28	0.16–4.64
Malignant melanoma of skin (172)	8	0.84	0.36–1.65	4	0.68	0.19–1.75	0	—	0.00–1.12
Central nervous system (191,192)	12	0.75	0.39–1.30	1	1.13	0.54–2.08	5	1.11	0.36–2.59
All lymphatic, hematopoietic tissue (200–209)	67	1.05	0.82–1.34	22	0.75	0.47–1.13	14	1.00	0.54–1.67
Hodgkin disease (201)	3	0.90	0.19–2.62	1	0.67	0.02–3.70	0	—	0.00–4.26
Non-Hodgkin lymphoma (200,202)	26	1.12	0.73–1.64	8	0.69	0.30–1.35	6	0.93	0.34–2.02
Leukemia, aleukemia (204–207)	25	1.01	0.65–1.49	10	0.90	0.43–1.66	6	1.23	0.45–2.68
Diabetes mellitus (250)	34	0.62*	0.43–0.87	12	0.46*	0.24–0.80	7	0.61	0.25–1.26
Cerebrovascular disease (430–438)	127	0.70*	0.58–0.83	29	0.59*	0.39–0.84	10	0.59	0.28–1.08
All heart disease (390–398,400.1,400.9, 402,404,410–414,420–429)	838	0.79*	0.73–0.84	225	0.60*	0.53–0.69	84	0.62*	0.49–0.76
Nonmalignant respiratory disease (460–519)	195	0.87*	0.75–1.00	58	0.80	0.61–1.04	9	0.40*	0.18–0.77
Cirrhosis of liver (571)	29	0.50*	0.34–0.72	13	0.43*	0.23–0.73	9	0.44*	0.20–0.84
Accidents (E800–E949)	96	0.89	0.72–1.09	41	0.70*	0.50–0.95	46	0.72*	0.53–0.97
Suicide (E950–E959)	46	1.02	0.75–1.36	7	0.28*	0.11–0.57	19	0.68	0.41–1.05
Homicides, other external causes (residual)	16	0.54*	0.31–0.88	4	0.17*	0.05–0.44	11	0.27*	0.14–0.48
Unknown causes of death	40	—	—	16	—	—	4	—	—

*$P < 0.05$.
[a]Expected number of deaths based on the Harris County (Texas) male population, ICD revision in effect at the time of death.

95% CI = 0.88–2.71) as was mortality from leukemia (SMR = 1.23, 95% CI = 0.45–2.68). One of the six people who had died from leukemia worked briefly at DPMC for less than 6 months; had this person been excluded from the analysis, the observed and expected deaths from leukemia would have been the same (5 observed and 4.9 expected).

To assess the possible effect of long-term employment, we also examined a subgroup of male employees (n = 5635) who worked for 10 or more years (Table 5). This group contributed 47% of the total person-years and 69% of deaths in the total cohort. Mortality from all causes combined (SMR = 0.78, 95% CI = 0.75–0.81) and from all malignant neoplasms (SMR = 0.91, 95% CI = 0.85–0.98) was again significantly decreased. Lung cancer mortality was significantly decreased among both the total population (SMR = 0.85, 95% CI = 0.75–0.97) and the refinery population (SMR = 0.84, 95% CI = 0.71–0.98). The SMR for lung cancer among chemical employees was also decreased but was not statistically significant (SMR = 0.88, 95% CI = 0.71–1.07). The cause-specific mortality pattern is virtually the same as that exhibited by the total cohort in Table 2. There were no significant excesses of any causes of death. Similar to the total cohort results, non-significantly elevated SMRs were noted among the refinery population for cancer of the rectum (SMR = 1.42, 95% CI = 0.71–2.54), Hodgkin disease (SMR = 1.36, 95% CI = 0.28–3.96), and non-Hodgkin lymphoma (SMR = 1.18, 95% CI = 0.72–1.83). Small and non-significant increases in mortality from cancers of the large intestine (SMR = 1.22, 95% CI = 0.80–1.77) and from leukemia (SMR = 1.22, 95% CI = 0.63–2.12) were noted among employees of the chemical plant.

TABLE 5
Observed Deaths and Standardized Mortality Ratios (SMRs)[a] of Male Employees Who Worked for ≥ 10 Years, 1948–2003

	Refinery (n = 3355; 94,160.9 person-yrs)			Chemical (n = 2280; 62,244.0 person-yrs)			Total (n = 5635; 156,404.8 person-yrs)		
Cause of Death (8th ICD revision code)	Observed	SMR	95% CI	Observed	SMR	95% CI	Observed	SMR	95% CI
All causes (001–999)	1638	0.82*	0.78–0.86	748	0.72*	0.67–0.77	2386	0.78*	0.75–0.81
All malignant neoplasms (140–209)	462	0.94	0.85–1.02	243	0.87*	0.77–0.99	705	0.91*	0.85–0.98
Buccal cavity, pharynx (140–149)	9	0.70	0.32–1.34	6	0.86	0.32–1.87	15	0.76	0.43–1.25
Digestive organs, peritoneum (150–159)	110	0.94	0.77–1.13	59	0.92	0.70–1.18	169	0.93	0.80–1.08
Esophagus (150)	12	0.96	0.49–1.67	5	0.67	0.22–1.56	17	0.85	0.49–1.36
Stomach (151)	12	0.75	0.39–1.31	5	0.63	0.21–1.48	17	0.71	0.41–1.14
Large intestine (153)	43	1.08	0.78–1.45	27	1.22	0.80–1.77	70	1.13	0.88–1.43
Rectum (154)	11	1.42	0.71–2.54	0	—	0.00–0.86	11	0.92	0.46–1.64
Biliary passages, liver primary (155,156)	13	0.91	0.48–1.55	7	0.83	0.33–1.71	20	0.88	0.54–1.36
Pancreas (157)	18	0.75	0.45–1.19	14	1.09	0.60–1.83	32	0.87	0.60–1.23
Respiratory system (160–163)	162	0.85*	0.72–0.99	98	0.89	0.72–1.08	260	0.86*	0.76–0.97
Bronchus, trachea, lung (162)	154	0.84*	0.71–0.98	93	0.88	0.71–1.07	247	0.85*	0.75–0.97
Prostate (185)	49	0.98	0.72–1.29	19	0.75	0.45–1.17	68	0.90	0.70–1.14
Kidney (189.0,189.2)	13	1.09	0.58–1.86	4	0.56	0.15–1.43	17	0.89	0.52–1.42
Bladder and other urinary organs (188,189.9)	13	1.01	0.54–1.73	3	0.47	0.10–1.36	16	0.83	0.47–1.35
Malignant melanoma of skin (172)	5	0.71	0.23–1.66	3	0.67	0.14–1.95	8	0.69	0.30–1.37
Central nervous system (191,192)	10	0.86	0.41–1.58	2	0.28	0.03–1.00	12	0.64	0.33–1.11
Cancer of all lymphatic, hematopoietic tissue (200–209)	48	1.06	0.78–1.41	26	0.99	0.65–1.46	74	1.04	0.81–1.30
Hodgkin disease (201)	3	1.36	0.28–3.96	0	—	0.00–3.33	3	0.90	0.19–2.64
Non-Hodgkin lymphoma (200,202)	20	1.18	0.72–1.83	7	0.68	0.27–1.40	27	0.99	0.65–1.44
Leukemia, aleukemia (204–207)	17	0.97	0.57–1.55	12	1.22	0.63–2.12	29	1.06	0.71–1.52
Diabetes mellitus (250)	25	0.64*	0.41–0.94	6	0.26*	0.09–0.56	31	0.50*	0.34–0.70
Cerebrovascular disease (430–438)	86	0.67*	0.54–0.83	38	0.66*	0.46–0.90	124	0.66*	0.55–0.79
All heart disease (390–398,400.1,400.9, 402,404,410–414,420–429)	592	0.78*	0.72–0.85	244	0.64*	0.57–0.73	836	0.74*	0.69–0.79
Nonmalignant respiratory disease (460–519)	131	0.83*	0.70–0.99	57	0.72*	0.55–0.94	188	0.80*	0.69–0.92
Cirrhosis of liver (571)	22	0.51*	0.32–0.77	9	0.35*	0.16–0.66	31	0.45*	0.31–0.64
Accidents (E800–E949)	59	0.82	0.62–1.06	30	0.72	0.49–1.03	89	0.78*	0.63–0.97
Suicide (E950–E959)	30	0.92	0.62–1.31	16	0.80	0.46–1.30	46	0.88	0.64–1.17
Homicides, other external causes (residual)	5	0.24*	0.08–0.57	5	0.35*	0.11–0.81	10	0.29*	0.14–0.52
Unknown causes of death	24	—	—	2	—	—	26	—	—

*$P < 0.05$.
[a]Expected number of deaths based on the Harris County (Texas) male population, ICD revision in effect at the time of death.

To further assess the possible effect of long-term employment, we also examined a subgroup of male employees (n = 3906) who worked for 20 or more years between 1948 and 2003 (data not shown). Mortality from all causes combined (SMR = 0.78, 95% CI = 0.74–0.82) and from all malignant neoplasms (SMR = 0.91, 95% CI = 0.83–0.99) was virtually identical to that of the group working for 10 or more years. However, mortality from cancer of the large intestine (SMR = 1.25, 95% CI = 0.95–1.62), as well as Hodgkin disease (SMR = 1.61, 95% CI = 0.33–4.72), non-Hodgkin lymphoma (SMR = 1.35, 95% CI = 0.88–1.98), and leukemia (SMR = 1.18, 95% CI = 0.75–1.77) was higher among employees working for 20 or more years, compared with that of employees working for 10 or more years.

Among female employees, mortality from all causes (SMR = 0.70, 95% CI = 0.54–0.91) and all malignant neoplasms (SMR = 0.68, 95% CI = 0.40–1.07) was decreased. Most of the cause-specific mortality was also decreased, including breast cancer (SMR = 0.50, 95% CI = 0.10–1.46), heart disease (SMR = 0.82, 95% CI = 0.49–1.30), nonmalignant respiratory disease (SMR = 0.86, 95% CI = 0.28–2.00), and all external causes of death (SMR = 0.52, 95% CI = 0.14–1.33). However, mortality from a number of cancer sites was non-significantly increased, including cancers of the lung (SMR = 1.50, 95% CI = 0.69–2.85) based on nine observed deaths, of all lymphatic and hematopoietic tissue (SMR = 1.30, 95% CI = 0.27–3.80) based on three deaths, and from non-Hodgkin lymphoma (SMR = 2.20, 95% CI = 0.27–7.96) based on two deaths (data not shown).

The mortality data that we used in the OCMAP program does not provide analyses for cell-type specific leukemia. Therefore, a separate anal-

TABLE 6
Observed and Expected Leukemia Deaths and Standardized Mortality Ratios (SMRs) of Male Employees According to Cell Type, 1948–2003

	Total			
Leukemia Cell Type	Observed	Expected[a]	SMR	95% CI
Total population				
Acute non-lymphocytic (ANLL)	12	12.41	0.97	0.50–1.69
Acute myelocytic (AML)	11	12.16	0.90	0.45–1.62
Chronic myelocytic (CML)	3	4.53	0.66	0.14–1.93
Acute lymphocytic (ALL)	3	1.81	1.66	0.34–4.84
Chronic lymphocytic (CLL)	9	7.88	1.14	0.52–2.17
Others	14	12.76	1.10	0.60–1.84
≥10 yrs of employment				
Acute non-lymphocytic (ANLL)	8	8.02	1.00	0.43–1.97
Acute myelocytic (AML)	7	7.84	0.89	0.36–1.84
Chronic myelocytic (CML)	2	2.87	0.70	0.08–2.52
Acute lymphocytic (ALL)	3	1.07	2.80	0.58–8.19
Chronic lymphocytic (CLL)	5	5.57	0.90	0.29–2.09
Others	11	8.76	1.26	0.63–2.25
≥20 yrs of employment				
Acute non-lymphocytic (ANLL)	7	5.85	1.20	0.48–2.46
Acute myelocytic (AML)	6	5.71	1.05	0.39–2.29
Chronic myelocytic (CML)	2	2.01	1.00	0.12–3.59
Acute lymphocytic (ALL)	2	0.74	2.70	0.33–9.76
Chronic lymphocytic (CLL)	4	4.27	0.94	0.25–2.40
Others	8	6.73	1.19	0.51–2.34

[a]Expected number of deaths based on the US male population, ICD revision in effect at the time of death.

ysis was carried out for acute non-lymphocytic leukemia (ANLL), acute and chronic myelocytic leukemia (AML, CML), and acute and chronic lymphocytic leukemia (ALL, CLL). There was no significant increase in mortality for any specific leukemia cell type (Table 6). For the total cohort, the observed numbers of deaths from ANLL and AML were the same or lower than the expected, with an SMR of 0.97 (95% CI = 0.50–1.69) and 0.90 (95% CI = 0.45–1.62), respectively. Similarly, for those who worked for more than 10 years, the SMR was 1.00 (95% CI = 0.43–1.97) for ANLL and was 0.89 (95% CI = 0.36–1.84) for AML. Mortality from ANLL was slightly elevated, with 7 observed and 6 expected deaths, among employees working for 20 or more years (SMR = 1.20, 95% CI = 0.48–2.46). The number of observed deaths for CLL was slightly higher in the total cohort (SMR = 1.14, 95% CI = 0.52–2.17) but was lower among those who worked for more than 10 years (SMR = 0.90, 95% CI = 0.29–2.09) or among those employees who worked more than 20 years (SMR = 0.94, 95% CI = 0.25–2.40). Based on only three deaths, there was no significant increase in mortality from ALL in the total population (SMR = 1.66, 95% CI = 0.34–4.84) and among employees who worked for 10 or more years (SMR = 2.80, 95% CI = 0.58–8.19) and 20 or more years (SMR = 2.70, 95% CI = 0.33–9.76).

Discussion

After more than half a century of follow up of employees with potential exposures to a variety of petroleum products and petrochemicals, this cohort continues to show a more favorable mortality experience than does the general population in Harris County, Texas. The overall mortality and all cancer mortality were 23% and 13% lower for the total study population, respectively. Because 35% of the male cohort members died during the study period and because most of the male cohort members were hired before 1960, with an average follow-up of 34 years, the mortality ratios for many causes of deaths are stable and representative. The 23% lower overall mortality of this population can be translated into longer life expectancy.[27] Based on the mortality experience of these employees, the life expectancy at age 25 among cohort members is estimated to be 2.6 years longer than their counterparts in the general population.

This study did not show an increase of any lymphatic or hematopoietic tissue cancer among employees working for 10 or more years. However, among employees working for 20 or more years, mortality from Hodgkin disease, non-Hodgkin lymphoma, and leukemia was non-significantly increased. Among the 23 cases of leukemia in workers employed for 20 or more years, 20 of the cases were hired before 1950 and 3 were hired between 1950 and 1955. Potential for benzene exposure or benzene-containing mixtures exists at every petroleum refinery complex.[4] High level and long duration of benzene exposure has been reported to be associated with ANLL and AML,[28–31] but evidence linking ALL, CML, or CLL to benzene exposure is lacking.[32] In this study, the observed numbers of ANLL and AML deaths were about the same as those expected, with SMRs approximately equal to or lower than 1. This observation might suggest that benzene exposures in the past at this facility might have been too low to cause an increase in ANLL or AML. ALL was non-significantly elevated based on three deaths. However, there is no obvious explanation for this increase. No epidemiological study has shown an association between exposure to benzene and ALL. The existing literature has also shown that ALL was not associated with refinery work.[22,24] Although a recent study has reported a statistical increase of ALL, the authors concluded that an occupational causa-

tion was unlikely.[8] There were also no increases of CML and CLL in the current study.

A non-significant increase of cancer of the large intestine was noted among employees hired after 1960. There were no increases of this cancer among employees hired either before 1950 or between 1950 and 1959. An increased risk of this cancer has not been noted in this industry.[1,3,11] A review of the individual work histories did not reveal any common work area, job assignments, or process operation for these 14 cases. The predominant jobs held included a variety of operations (phenol acetone, olefins, catalytic cracking, lubricant, shipping, epichlorohydrin, and alkylation), maintenance (control systems, field engineering, welding, instrument systems, pipefitting, and engineering services), and laboratory (technical-chemical laboratory positions). Thus, the non-significant increase of this cancer is likely a chance occurrence rather than associated with potential exposures at this facility. The average age at hire was 37 years, and median duration of employment was 10 years.

A noticeable finding from the previous study was a 2-fold increase in mesothelioma mortality.[7] The increase in mesothelioma deaths is indicative of asbestos exposure.[33–35] Of the causes of death examined in this update study, mesothelioma is the only condition showing a statistically significant increase. A total of 21 deaths from mesothelioma were found, 14 of which were identified during the update period from 1990 to 2003. Several other studies of petroleum workers have reported an increase of this disease and have attributed this increase to the past asbestos exposure.[2,7,9,12,17,36–39] Depending on the study design and the proportion of study subjects potentially exposed to asbestos, the SMR for mesothelioma among petroleum industry workers ranges from approximately 2 in a recent Australian study[17] to more than 8 in a Canadian refinery cohort.[12] The increased risk of mesothelioma was particularly profound among those who had maintenance jobs,[37,40] especially for those employed as insulators.[34,37]

Sixteen of the 21 people with mesothelioma started working at DPMC before 1950, four started between 1951 and 1953, and one person started in the early 1970s. The SMR for those who starting working before 1950 was 3.18 (95% CI = 1.82–5.15), whereas among employees hired since 1950, the SMR was 1.48 (95% CI = 0.48–3.46). An examination of their work histories reveals that two thirds (n = 14) of the 21 workers had been employed in maintenance positions, which had the greatest potential for asbestos exposure. Among workers with mesothelioma who starting working at DPMC after 1950, one had worked as a pipefitter (one of the jobs with greatest potential for exposure to asbestos) for 5 years at another refining facility during the early 1950s. His DPMC career started in the early 1970s, where he worked in a non-maintenance position for less than 10 years. Excluding this case, the observed and expected numbers of deaths from mesothelioma among those beginning work at DPMC after 1950 would have been no different (4 vs 3.4, with an SMR of 1.18).

In the subgroup of male employees who had worked in maintenance jobs for a minimum of 1 year, the jobs included insulators, pipefitters, boilermakers, electricians, welders, carpenters, and laborers. Maintenance work covers a broad range of activities, principally repairing, replacing, or modifying process equipment and related structures. The type of work with the greatest potential exposure to asbestos has been the removal, repair, or reapplication of asbestos-containing thermal insulation. It is to be noted that non-asbestos insulation has been used for reapplication since the early to mid 1970s. A more detailed description of maintenance work at this facility has been reported previously.[40]

The overall mortality in the maintenance subgroup was favorable compared to that of the population of Harris County. Cancer mortality was 8% to 10% lower, which was borderline significant. The observed numbers of deaths as a result of cancers of the digestive system, including stomach, large intestine, rectum, and other specific sites, were lower than or similar to those expected; none of the SMRs were significantly lower or higher than 1. Although positive associations of these cancers have been suggested in some studies,[34–35,41–43] other studies have not shown an effect.[44–48] Only mortality from mesothelioma showed a statistically significant increase, and that was seen among employees who had worked at least 1 year in maintenance jobs and among the group of employees with 10 or more years in potentially exposed jobs with 20 years since their first maintenance job at DPMC.

One weakness in our assessment of mesothelioma was the lack of information about jobs before joining or after leaving the facility, or both. Of the 13 deaths from mesothelioma identified in the maintenance group at Deer Park, previous work histories were available for only 6 of them. Notably, two employees had worked as pipefitters, one at a shipyard and the other at another refinery. Both workers had potential exposure to asbestos, particularly the one who worked for the shipyard, where he likely encountered significantly greater asbestos exposure before working at DPMC.

The lack of increase of lung cancer among employees who had the greatest potential for asbestos exposure in this population has been documented previously.[40] Similar findings have also been reported in many other studies on petroleum workers.[9,17,37] This observation might suggest that mesothelioma can be induced at a lower cumulative exposure than is needed for induction of lung cancer, although other factors may also play a role.[40]

In summary, after more than half a century of follow-up, employees at this facility continue to show a more favorable mortality than does the general local population. Although mortality from leukemia associated with benzene exposure in this industry has been a concern, no statistically significant increase of overall leukemia or any of the specific cell types was found. The increased rate of mesothelioma is probably related to past exposure to asbestos, since the latent period for this disease is approximately 40 years. The nonsignificant increase of cancer of the large intestine is likely a chance occurrence after reviewing the detailed individual work histories.

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