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Critical Review of Cancer Epidemiology in Petroleum Industry Employees, With a Quantitative Meta-Analysis by Cancer Site

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A critical review of close to 100 published and unpublished but otherwise available epidemiologic reports of petroleum industry employees from the United States, United Kingdom, Canada, Europe, Australia, and Japan was conducted. Analyses by duration of employment and latency are discussed, and summary standardized mortality ratios (SMRs) or meta-SMRs are developed for selected cancer sites. Findings indicate that the industry experienced a significantly lower cancer mortality than the general population for all cancer sites combined, digestive system, stomach, and lung. For the industry as a whole, SMRs similar to the general population were observed for skin, brain, pancreatic, prostatic, and kidney cancers. However, some data indicate that certain small groups within the industry might have elevated prostatic and kidney cancer risk. This review supports the conclusion that some refinery employees, particularly those employed before the 1940s, may have been at increased risk of leukemia. There is some indication that cancer of other lymphatic tissue may also be elevated. Unresolved issues affecting these conclusions are discussed, and specific directions for future research are offered.

Key words: occupational cancer, petroleum, gasoline, benzene, meta-analysis, meta-SMR

INTRODUCTION

A large number of epidemiologic studies of workers in the petroleum industry have been conducted. Although these studies differ in design, size, and length of follow-up, they examine the mortality pattern of workers with similar exposures, including refinery process streams chemically similar in composition to commercial gasoline. These workers were exposed to a higher concentration and for a longer duration than the general public. Therefore, these studies represent the best available data on human effects of exposure to gasoline hydrocarbons.

Although several epidemiologic reviews have appeared [Raabe, 1983; Savitz and Moure, 1984; EPA, 1987; Harrington, 1987], none of these reviews examined the complete literature systematically or provided a quantitative meta-analysis. The

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purpose of this review is to examine critically this literature and to develop a quantitive assessment (meta-analysis) of the site-specific cancer mortality patterns that emerge from these studies.

Close to 100 published articles and unpublished but otherwise available reports from the United States, United Kingdom, Canada, Europe, Australia, and Japan have been reviewed. Particular attention has been directed toward the appropriateness and adequacy of study design, study subject selection, exposure data, and follow-up of study subjects. Since we are dealing with the assessment of carcinogenicity of industrial chemicals, the most appropriate study design is that of a retrospective or historical cohort mortality study. In a cohort study, the population at risk is defined, and the exposures (at least in general terms) are relatively well documented. Furthermore, mortality is a valid endpoint for most cancer sites. In addition to study design and data quality, statistical methods have been examined, as well as the validity of interpretations and conclusions. Our assessment is based on relevant and appropriate studies. A number of articles were not included in the final assessment because they were found to be inappropriate or inadequate.

We will first describe briefly the studies used in this review. Table I provides some of the basic information for the studies reviewed: company, location of facility, length and period of follow-up, minimum length of employment for cohort eligibility, cohort size, person-years, and the number of deaths. A full report with a summary and comments on each study is available upon request.

In the United States, the first large-scale industrywide cohort mortality study in the petroleum industry was sponsored by the American Petroleum Institute (API) and conducted by Tabershaw/Cooper Associates [TCA, 1974]. Based on this study, Wong [1980] reported an analysis of brain tumor mortality, which was not included in the original TCA report. Subsequently this API refinery study was updated from 1971 to 1980 [Kaplan, 1986]. Also under the sponsorship of API was the Memorial Sloan Kettering Cancer Center (MSKCC) registry of mortality and cancer incidence of 19 oil companies. The results of the first three years of data were reported by Schottenfeld et al. [1981].

A large number of studies on refinery workers have been conducted or sponsored by individual oil companies in the United States. Although the majority of the studies were historical cohort mortality studies in design, a small number of studies was actually based on a limited length of follow-up. From the methodological point of view, these studies fall into a hybrid category between the traditional cohort (longitudinal) study and a cross-sectional survey.

The individual company studies that fall into the hybrid category include the AMOCO companywide study [Nelson, 1985]; the Exxon study of the Baton Rouge refinery [Hanis et al., 1982]; the Exxon study of the Baton Rouge, Baytown, and Bayway refineries and chemical plants [Hanis et al., 1985a,b]; and the two Shell studies of the Wood River [McCraw et al., 1985] and Deer Park [Joyner, 1983] refineries. As indicated in Table I, the follow-up was relatively short for these studies with the hybrid design. In most cases, the start date of the follow-up period coincided with the date of the computerization of personnel records. This type of study, although limited from a methodological point of view, was relatively quick and less expensive.

The traditional cohort mortality study, with a much longer follow-up, requires the time-consuming task of manually coding both the demographic and work history

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TABLE I. Description of Cohort Studies in the Petroleum Industry

Author/year	Company	Facility	Follow-up period	Length years	Minimum employment	Cohort size	Person years	Total deaths
Tabershaw Cooper Assc. [1974]	Industrywide	17 refineries	1962-1971	10	1 + years	20,163	137,153	1,165
Wong [1980]	Industrywide	17 refineries	1962-1971	10	1 + years	20,163	137,153	1,165
Kaplan [1986]	Industrywide	17 refineries	1962-1980	19	1 + years	20,163	297,591	3,349
Schottenfeld et al. [1981]	19 companies	Refineries and other facilities	1977-1979	3	none	55,007	122,607	502
Nelson [1985]	AMOCO	10 refineries	1970-1982	13	6 + months	10,761	104,954	983
Wong et al. [1986]	Chevron	Richmond, El Segundo Refineries	1950-1980	31	1 + years	14,179	266,470	2,292
Hams et al. [1982]	Exxon	Baton Rouge Refinery	1970-1977	8	1 + month	8,666	52,791	1,199
Hams et al. [1985a]	Exxon	Baton Rouge, Baytown, Bayway Refineries	1970-1977	8	1 + months	21,698	137,702	3,198
Wen et al [1983]	Gulf	Port Arthur Refinery	1937-1978	42	None	15,095	372,505	4,269
Wen et al [1984c]	Gulf	Port Arthur Refinery	1937-1983	47	None	15,095	427,394	5,470
Morgan and Wong[1984]	Mobil	Beaumont Refinery	1945-1979	35	1 + years	6,139	123,354	1,582
Morgan and Wong[1985]	Mobil	Paulsboro Refinery	1946-1979	34	1 + years	4,263	93,434	1,164
Enterline and Henderson [1985]	Mobil	Torrance Refinery	1959-1978	20	1 + years	1,621	23,154	250
McCraw et al [1985]	Shell	Wood River Refinery	1973-1982	10	None	3,976		640
Joyner [1983]	Shell	Deer Park Refinery	1973-1981	9	None			237
Divine et al [1985]	Texaco	13 refineries + other facilities	1947-1977	31	5 + years	19,077	358,029	4,024
Divine and Barron [1987]	Texaco	Production + pipeline	1946-1980	35	6 + months	11,098	220,414	1,886
Rushton and Alderson [1981a]	Industrywide	8 UK refineries	1950-1975	26	1 + years	34,781	575,982	4,406
Rushton and Alderson [1983]	3 companies	UK distribution centers	1950-1975	26	1 + years	23,806	397,569	3,926
Hams et al [1979]	Imperial Oil	Refineries and other facilities	1964-1973	10	5 + years	15,032	82,057	1,511
Theriault and Goulet [1979]	Shell Canada	East Montreal Refinery	1928-1975	48	5 + years	1,205		
Theriault and Provencher [1987]	Shell Canada	East Mongreal Refinery	1928-1981	54	5 + years	1,207	25,224	175
Christie [1987]	Industrywide	Oil companies in Australia	1981-1986		65 + years	10,489	40,214	133
Nakamura [1987]	Industrywide	51 Japanese refineries	1961-1981	21	3 + years	19,475	19,476	451

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information of the cohort members, usually in the range of several to tens of thousands. Included in this category are the studies of the Chevron Richmond and El Segundo refineries [Wong et al., 1986]; the Gulf Port Arthur refinery [Wen et al., 1983, 1984a]; the Mobil Beaumont [Morgan and Wong, 1984], Paulsboro [Morgan and Wong, 1985], and Torrance refineries [Enterline and Henderson, 1985]; and the Texaco companywide study [Divine et al., 1985; Divine and Barron, 1986, 1987].

These cohorts have also generated a number of reports based on specific subcohort analyses. For example, the Gulf Port Arthur data were the bases for two subcohorts: employees assigned to the benzene [Tsai et al., 1983] and to the MEK dewaxing units [Wen et al., 1985]. Based on the cohort data, a few nested case-control studies have also been conducted. An example was the leukemia study on the Shell employees at the Wood River refinery [Austin et al., 1986].

In Britain, an industrywide study of eight refineries was conducted [Rushton and Alderson, 1981a]. A subsequent case-control study of leukemia was carried out within this cohort [Rushton and Alderson, 1981b]. A study consisting of employees at the distribution centers of three companies in England was also conducted by the same investigators [Rushton and Alderson, 1983].

There are also a number of cohort mortality studies of refinery workers from Canada, Australia, and Japan. Hanis et al. [1979] reported the mortality experience of the Imperial Oil (Canada) employees at several refineries and other facilities. The Thériault and Goulet [1979] report was based on the mortality experience of the Shell East Montreal refinery, which was subsequently updated by Thériault and Provencher [1987]. The Australian study was based on the first 3 years of mortality data accumulated in the prospective registry in the petroleum industry sponsored by the Australian Petroleum Institute [Christie, 1987]. Finally, a brief report from Japan described the results of a mortality study of Japanese petroleum workers sponsored by the Petroleum Association of Japan [Nakamura, 1987].

The studies described above have been reviewed in detail. However, because of the limited space available, detailed comments on specific studies will not be discussed here. Because of the study design, the defined population at risk, the availability of mortality rates, the defined exposures, and the completeness and length of follow-up, these studies were judged to be adequate methodologically and to be of sufficient quality to form the basis of our assessment below.

A number of studies that we have reviewed were excluded from our assessment because of various serious limitations. Several studies that fell into this category were proportional mortality ratio (PMR) studies based totally on death certificates available to union locals [Thomas et al., 1980; Thomas et al., 1982a; Reeve et al., 1982]. In addition to the well-known methodological deficiencies of PMR studies [Wong and Decouflé, 1982; Wong et al., 1985], these particular studies also suffered from incomplete ascertainment of deaths [Wong and Tabershaw, 1980]. For example, in the Reeve et al. [1982] study, deaths were identified through local union death notifications, obituaries, word of mouth, and lists of surviving families to whom bibles were sent. In the Thomas et al. [1980] study, it was stated that death certificates for 10% of the deaths identified were not retrieved. Furthermore, employment histories were not available for these PMR studies, and the analyses were limited. Finally, the refineries included in these PMR studies have subsequently been studied thoroughly with the cohort study design by individual companies. Based on these considerations, these PMR studies were not included in our assessment.

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Two company-sponsored studies were also excluded from our assessment because of methodological or data deficiencies. The study conducted by Baird [1967] on Humble Oil (Exxon) employees was very crude judging by today's standard. The number of deaths reported in that study was likely incomplete, and the estimate of employees at risk was most likely inaccurate. The Thorpe [1974] study of eight Esso European facilities was likewise based on incomplete death ascertainment and inaccurate estimate of population at risk.

In addition to studies conducted on employees in the petroleum industry, there are also a number of population-based case-control studies that included petroleum or petroleum-related occupations in the analysis [McLaughlin et al., 1984; Mommsen et al., 1983; Lin and Kessler, 1981; McLaughlin et al., 1985; Howe et al., 1980; Stemhagen et al., 1983]. The relationship between various occupations and cancers of the bladder, kidney, pancreas, and liver was investigated in these studies. None of these studies provided adequate information about the nature of exposure or details of employment. Methodological problems (such as control selection, recall of employment histories, adjustment of confounding factors in analysis) further complicated the interpretation. With the exception of the concern for kidney cancer raised by the API animal work [MacFarland et al., 1984], none of these cancer sites has been implicated by occupational studies. These studies were excluded from our final assessment.

RISK ASSESSMENT BY CANCER SITE

In this section, we summarize the epidemiologic data from the cohort mortality studies on petroleum workers by individual cancer site. If a study had been updated, the updated data were used. Industrywide studies are not included in the data summarization, since part of the data overlap those in individual company studies. Subcohort analyses are not included in the data summarization either, since the data for the entire study are utilized.

In evaluating the data for causal relationship, some of the criteria set forth by Hill [1965] are used. In particular, we emphasize, to the extent possible, the strength of association, consistency of findings, and dose-response relationship. However, our application of Hill's criteria is limited by the data available from the original studies. An overall index for strength of association is a summary standardized mortality ratio (SMR) or meta-SMR based on all the available appropriate data. A method of calculating the summary SMR or meta-SMR is given below. In terms of dose-response relationship, the issue is more complicated. Most of the studies did not provide any dose-response analysis. Few industrial hygiene data existed in the industry prior to the mid-1970s, whereas relevant exposures occurred much earlier. In some studies, broad exposure categories were used. Some used length of employment as a surrogate for length of exposure. Even for these latter studies, the groupings were so different that no quantitative summarization can be done without access to the original data. Thus, dose-response results can only be used in a qualitative manner in our assessment.

The statistical procedure for data summarization (meta-analysis) consists of summing up the observed and the expected deaths for a specific cancer site from all eligible studies and calculating the summary SMR or meta-SMR. (The Hanis et al. [1979] study utilizing the direct method of standardization could not be included in this procedure.) This simple procedure treats each study as a separate metastratum in

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the data summarization, thus "adjusting" for individual studies while preserving the original adjustment using substrata specific to age, sex, race, calendar year, and country. The summary or meta-SMR is automatically weighted by the size of the individual studies (observed and expected deaths). Chi-squares are calculated to test the significance of the summary SMR. Ninety-five percent confidence intervals are also calculated for the summary SMR (presented in the last table). Similar procedures have been used in summarizing data in several epidemiologic reviews: asbestos and gastrointestinal cancer [Morgan et al., 1985], artificial sweeteners and bladder cancer [Morgan and Wong, 1985], formaldehyde and respiratory cancer [Nelson et al., 1986], chemical dyes and bladder cancer [Matanoski and Elliott, 1981], and radiation and colon cancer [Day, 1985]. In particular, this method was discussed in the interpretation of negative epidemiological evidence for carcinogenicity by the International Agency for Research on Cancer [Wald and Doll, 1985]. Although other statistical procedures for meta-analysis are available, the meta-SMR procedure is used in this review because of its simplicity in computation and interpretation, its preservation of the adjustments in the original studies, and its resemblance to the analyses in the original studies.

An additional benefit of meta-analysis is that it comprehends the multiple-comparison problem exhibited in these cohort studies. Most of the cohort studies that we reviewed examined over 40 individual cancer sites each. Statistically significant results for as many as two sites could have occurred by chance alone given a 95% confidence level. By our examination of these multiple sites across these studies, chance excesses or deficits for a particular cancer site in individual studies are less likely to influence the overall interpretation.

Since the summary SMR is based on the expected deaths derived from national mortality statistics in the original studies, the issue of appropriateness of applying national rates to specific locales applies to the meta-analysis in this review as well. To be consistent with the data presented in the original papers, we have kept two decimal places in the expected numbers of deaths.

Although the summary SMR gives an overall risk index for the industry as a whole, it has the disadvantage of dilution. If the risk is low and affects only a small portion of the employees instead of the entire industry, an overall summary index may not be sensitive. Therefore, data from each study have to be examined for any dose-response relationship and any significant risk for any subcohort. Unfortunately, few studies provided analysis by length of employment on a comprehensive basis, i.e., for all causes of death. Those reporting comprehensive analysis by length of employment included the Chevron Richmond and El Segundo refineries [Wong et al., 1986], the Mobil Beaumont refinery [Morgan and Wong, 1984], the Mobil Paulsboro refinery [Morgan and Wong, 1985], and the Mobil Torrance refinery [Enterline and Henderson, 1985]. Length of employment analysis was done for a few selected causes of death in the Gulf Port Arthur study and in the Texaco study. Rushton and Alderson reported length of employment analysis for selected causes of death as well as selected subcohorts in the British refinery and distribution center studies.

In addition to length of employment analysis, another analysis that is helpful in establishing an epidemiologic association is an examination of the data by latency or time since first exposure (usually first employment as a surrogate). Studies providing this type of analysis on a comprehensive basis included the Chevron study, the Mobil studies, and the Shell Canada [Thériault and Provencher, 1987] study. Both the Gulf

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TABLE II. Summary of Mortality From Cancer of All Sites in Cohort Studies of Refinery and Other Petroleum Employees[a]

Author/year	Facility	Observed deaths	Expected deaths	SMR	Statistical significance	Latency analysis	Duration analysis
Facershaw Cooper Assc [1974][a]	17 refineries	265	327.52	0.80	f		
Wong [1990][a]	17 refineries						
Kaplan [1946][a]	17 refineries	793	915.59	0.87	f		
Schottenfeld et al. [1981][a,b]	U.S. refineries	127	168.77	0.75	f		
Nelson [1985]	10 refineries	273	330.10	0.83	e		
Wong et al. [1986]	Richmond, El Segundo Refineries	462	610.70	0.75	f	c,d	c,d
Harris et al. [1992][a]	Baton Rouge Refinery	249	270.40	0.92			
Harris et al. [1985a]	Baton Rouge, Baytown, Bayway Refineries	666	705.00	0.94			
Wen et al. [1983][b]	Port Arthur Refinery	664	681.54	0.97			
Morgan and Wong [1984]	Beaumont Refinery	346	360.27	0.96		c,d	c,d
Morgan and Wong [1985]	Paulsboro Refinery	243	265.24	0.91		c,d	c,d
Enterline and Henderson [1985]	Torrance Refinery	56	69.32	0.80		c,d	c,d
McCraw et al. [1985]	Wood River Refinery	161	177.00	0.91			
Joyner [1983]	Deer Park Refinery						
Divine et al. [1985]	13 refineries & others	767	1,019.40	0.75	f		
Divine and Barrow [1987]	Production & pipeline	393	581.10	0.68	f	c,d	c,d
Rushton and Alderson [1981a]	8 UK Refineries	1,147	1,286.40	0.89	f		c,d
Rushton and Alderson [1983]	UK distribution centers	1,002	1,156.70	0.87	f		
Theriault and Goulet [1979][a]	East Montreal Refineries	25	28.54	0.88		c,d	
Theriault and Provencher [1987]	East Montreal Refineries	39	48.82	0.79		c,d	
Christie [1986]	Australia	52	56.90	0.91			
Nakamura [1987]	51 Japanese Refineries	134	176.80	0.76	f		
Total		6,405	7,525.29	0.85	($p < .00001$)		

[a]Note: Blank entries indicate that the observed and expected deaths are not reported by the authors.
[b]Excluded from the calculation of summary SMR.
[c]Only refinery employees are included.
[d]Only male hourly employees with 1 or more years of employment are included.
[e]Analysis done.
[f]$p < .05$
[g]$p < .01$.

and the Texaco studies included some latency analysis by specific causes of death. Finally, several studies [TCA, 1974; Wong et al., 1986; Wen et al., 1984a; Rushton and Alderson, 1981a, 1983] provided some analyses by hire date.

Cancer of All Sites Combined (ICD8, 140–209)

Table II presents the observed and expected deaths and the corresponding SMRs for cancer of all sites from the eligible cohort mortality studies of petroleum employees from the United States, Canada, Great Britain, Australia, and Japan. The all-cancer SMR ranged from 0.68 ($p < .01$) for Texaco production and pipeline employees to 0.97 for Gulf Port Arthur male workers. No study found any excess or trend (significant or otherwise) for all cancer. In fact, most of the larger studies demonstrated significant deficits for all cancer. The deficit was quite consistent for all the studies. The all-cancer meta-SMR based on 6,405 deaths was 0.85 ($p < .00001$), significantly lower than the general population.

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TABLE III. Summary of Mortality From Digestive Cancer in Cohort Studies of Refinery and Other Petroleum Employees[a]

Author/year	Facility	Observed deaths	Expected deaths	SMR	Statistical significance	Latency analysis	Duration analysis
Tabersnaw Cooper Assc [1974][a]	17 refineries	31	95.71	0.84			
Wong [1980][a]	17 refineries						
Kaplan [1986][a]	17 refineries	233	246.91	0.90			
Schottenfeld et al. [1981][a,b]	U.S. refineries	31	41.12	0.75			
Nelson [1985]	10 refineries	97	82.30	1.17			
Wong et al. [1986]	Richmond, El Segundo Refineries	125	174.62	0.71	e	x[d]	x[d]
Hanis et al. [1982][a]	Baton Rouge	73	74.90	0.97			
Hanis et al. [1985a]	Baton Rouge, Baytown, Bayway Refineries	196	195.30	1.00			
Wen et al. [1983][c]	Port Arthur Refinery						
Morgan and Wong [1984]	Beaumont Refinery	86	113.04	0.76	e	x[d]	x[d]
Morgan and Wong [1985]	Paulsboro Refinery	80	80.90	0.98		x[d]	x[d]
Enterline and Henderson [1985]	Torrance Refinery	10	18.30	0.54		x[d]	x[d]
McCraw et al. [1985]	Wood River Refinery						
Joyner [1983]	Deer Park Refinery						
Divine et al. [1985]	13 refineries & others	215	306.80	0.70	e		
Divine and Barron [1987]	Production & pipeline	105	168.70	0.62	e	x[d]	x[d]
Rushton and Alderson [1981a]	8 UK refineries						
Rushton and Alderson [1983]	UK distribution centers						
Theriault and Goulet [1979][a]	East Montreal Refinery	12	10.22	1.17		x[d]	
Thériault and Provencher [1987]	East Montreal Refinery	18	18.20	0.98		x[d]	
Christie [1986]	Australia	15	16.70	0.90			
Nakamura [1987]	51 Japanese refineries						
Total		947	1,174.86	0.81	($p<.00001$)		

[a]Note: Blank entries indicate that the observed and expected deaths are not reported by the authors.
[b]Excluded from the calculation of summary SMR.
[c]Only refinery employees are included.
[d]Only male hourly employees with 1 or more years of employment are included.
[e]x = Analysis done.
[f]$p < .01$.

Digestive Cancer (ICD8, 150–159)

For digestive cancer, four studies showed a significant deficit (Table III). Of all the studies listed in Table III, only one study, the AMOCO companywide study, showed a slight nonsignificant excess (SMR = 1.17). A closer examination of the AMOCO data indicated that out of the ten refineries investigated, the digestive cancer excess came from only one refinery (Whiting) and among employees hired before 1940. This isolated finding was not consistent with the rest of the data. For the industry as a whole, the digestive cancer meta-SMR was 0.81 (947 deaths observed), significant at the .00001 level.

Stomach Cancer (ICD8, 151)

Table IV presents stomach cancer SMRs from the eligible cohort mortality studies. No study detected any significant excess. The stomach cancer SMRs ranged from 0.39 ($p < .01$) for Texaco production and pipeline workers to 1.60 (not significant, $p = .20$) for the Shell Canada East Montreal refinery, where seven

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TABLE IV. Summary of Mortality From Stomach Cancer in Cohort Studies of Refinery and Other Petroleum Employees

Author/year	Facility	Observed deaths	Expected deaths	SMR	Statistical significance	Latency analysis	Duration analysis
Tabershaw Cooper Assc [1974][a]	17 refineries						
Wong [1980][a]	17 refineries						
Kaplan [1986][a]	17 refineries	43	44.06	0.98			
Schottenfeld et al. [1981][a,b]	U.S. refineries	6	5.95	1.00			
Nelson [1985]	10 refineries	17	11.90	1.43			
Wong et al. [1986]	Richmond, El Segundo Refineries	26	34.10	0.76		[d]	[d]
Hanis et al. [1982][a]	Baton Rouge Refinery	11	13.70	0.80			
Hanis et al. [1985a]	Baton Rouge, Baytown, Bayway Refineries	33	34.30	0.96			
Wen et al. [1983][c]	Port Arthur Refinery	63	56.69	1.11			
Morgan and Wong [1984]	Beaumont Refinery	24	26.55	0.90		[d]	[d]
Morgan and Wong [1985]	Paulsboro Refinery	14	17.56	0.79		[d]	[d]
Enterline and Henderson [1985]	Torrance Refinery	4	3.36	1.18		[d]	[d]
McCraw et al. [1985]	Wood River Refinery						
Joyner [1983]	Deer Park Refinery						
Divine et al. [1985]	13 refineries & others	45	63.90	0.70	e		
Divine and Barron [1987]	Production & pipeline	13	33.00	0.39	f	[d]	[d]
Rushton and Alderson [1981a]	8 UK refineries	167	160.86	1.04			[d]
Rushton and Alderson [1983]	UK distribution centers	123	144.47	0.85			
Theriault and Goulet [1979][a]	East Montreal Refinery						
Theriault and Provencher [1987]	East Montreal Refinery	7	4.36	1.60		[d]	
Christie [1986]	Australia						
Nakamura [1987]	51 Japanese refineries	49	68.90	0.71	e		
Total		585	659.95	0.89	($p < .005$)		

[a]Note: Blank entries indicate that the observed and expected deaths are not reported by the authors.
[b]Excluded from the calculation of summary SMR.
[c]Only refinery employees are included.
[d]Only male hourly employees with 1 or more years of employment are included.
[d]x = Analysis done.
[e]$p < .05$.
[f]$p < .01$.

stomach deaths were observed and 4.36 were expected. The East Montreal investigation [Thériault and Provencher, 1987] was a very small study with only 1,207 employees. Another Canadian study based on Imperial Oil employees [Hanis et al., 1979] detected a significant relative risk of esophageal and stomach cancer among the exposed employees when compared to the nonexposed employees (not shown in Table IV); the excess came from refineries in Ontario and Quebec. Exposure classification in this study was based on partial employment histories (post-1964); therefore, misclassification was likely, and analysis based on job or exposure categories was subject to error. In both Canadian studies, the stomach cancer excess came primarily from Quebec. The possibility of a confounding factor associated with that region should be investigated. In the United States, Nelson [1985] found a nonsignificant stomach cancer excess in AMOCO employees (SMR = 1.43). Similar to the finding in total digestive cancer, the stomach cancer excess came from the AMOCO Whiting refinery and among men hired before 1940.

On the other hand, the two Texaco studies found significant deficits in stomach

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TABLE V. Summary of Mortality From Pancreatic Cancer in Cohort Studies of Refinery and Other Petroleum Employees[a]

Author year	Facility	Observed deaths	Expected deaths	SMR	Statistical significance	Latency analysis	Duration analysis
Tabershaw Cooper Assc [1974][a]	17 refineries						
Wong [1980][a]	17 refineries						
Kaplan [1986][a]	17 refineries	44	51.25	0.86			
Schottenfeld et al. [1981][a,b]	U.S. refineries	10	8.85	1.12			
Nelson [1985]	10 refineries	18	17.00	1.05			
Wong et al. [1986]	Richmond, El Segundo Refineries	20	33.78	0.59	c	x[d]	x[d]
Harris et al. [1982][a]	Baton Rouge Refinery	23	15.10	1.52			
Harris et al. [1985a]	Baton Rouge, Baytown, Bayway Refineries	42	39.20	1.07			
Wen et al. [1983][c]	Port Arthur Refinery	37	37.80	0.99			
Morgan and Wong [1984]	Beaumont Refinery	23	20.14	1.14		x[d]	x[d]
Morgan and Wong [1985]	Paulsboro Refinery	15	14.81	1.01		x[d]	x[d]
Enterline and Henderson [1985]	Torrance Refinery	3	3.96	0.75		x[d]	x[d]
McCraw et al. [1985]	Wood River Refinery						
Joyner [1983]	Deer Park Refinery						
Divine et al. [1985]	13 refineries & others	62	57.70	1.07			
Divine and Barron [1987]	Production & pipeline	27	32.00	0.84		x[d]	x[d]
Rushton and Alderson [1981a]	8 UK refineries	50	51.55	0.97			
Rushton and Alderson [1983]	UK distribution centers	39	46.89	0.83			
Thériault and Goulet [1979][a]	East Montreal Refinery						
Thériault and Provencher [1987]	East Montreal Refinery						
Christie [1986]	Australia						
Nakamura [1987]	51 Japanese refineries						
Total		336	354.83	0.95	(p = .32)		

[a]Note: Blank entries indicate that the observed and expected deaths are not reported by the authors.
[b]Excluded from the calculation of summary SMR.
[c]Only refinery employees are included.
[d]Only male hourly employees with 1 or more years of employment are included.
[e]x = Analysis done.
[f]$p < .05$.

cancer; the SMR was 0.70 in the refinery employees and 0.39 in the production and pipeline employees. The Japanese industrywide study also found a significant deficit of stomach cancer. Mortality deficits from stomach cancer were also found in other studies. As Table IV indicates, the Chevron Richmond and El Segundo refineries and the Mobil Paulsboro refinery showed a modest deficit in stomach cancer. Rushton and Alderson [1983] found a lower than expected stomach cancer mortality in distribution workers (SMR = 0.85, p = .05, borderline significance).

Summing over all the eligible studies, the stomach cancer meta-SMR was 0.89 (585 observed deaths, $p < .005$). Thus, taking all studies into consideration and weighting the finding of each study by its sample size, the petroleum industry as a whole demonstrated a significantly lower stomach cancer mortality.

Pancreatic Cancer (ICD8, 157)

Mortality from pancreatic cancer among refinery workers is summarized in Table V. Most studies reported an SMR around 1. Wong et al. [1986] reported a

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TABLE VI. Summary of Mortality From Lung Cancer in Cohort Studies of Refinery and Other Petroleum Employees[a]

Author/year	Facility	Observed deaths	Expected deaths	SMR	Statistical significance	Latency analysis	Duration analysis
Tidewater Cooper Assc [1974][a]	17 refineries	90	112.71	0.79	f		
Wong [1980][a]	17 refineries						
Kaplan [1986][a]	17 refineries	270	317.72	0.85	e		
Schottenfeld et al. [1981][a,b]	U.S. refineries	48	65.07	0.73	e		
Nelson [1985]	10 refineries	77	125.90	0.61	f		
Wong et al. [1986]	Richmond, El Segundo Refineries	124	185.42	0.66	f	x[d]	x[d]
Hanis et al. [1982][a]	Baton Rouge Refinery	78	85.30	0.91			
Hanis et al. [1985a]	Baton Rouge, Baytown, Bayway Refineries	209	219.80	0.95			
Wen et al. [1983][c]	Port Arthur Refinery	182	183.22	0.99			
Morgan and Wong [1984]	Beaumont Refinery	101	100.11	1.00		x[d]	x[d]
Morgan and Wong [1985]	Paulsboro Refinery	61	76.38	0.79		x[d]	x[d]
Enterline and Henderson [1985]	Torrance Refinery	24	23.86	1.00		x[d]	x[d]
McCraw et al. [1985]	Wood River Refinery						
Joyner [1983]	Deer Park Refinery						
Divine et al. [1985]	13 refineries & others	182	306.00	0.59	f		
Devine and Barron [1987]	Production & pipeline	109	179.00	0.61	f	x[d]	x[d]
Rushton and Alderson [1981a][a]	8 UK refineries	416	532.70	0.78	f		
Rushton and Alderson [1983]	UK distribution centers	384	482.83	0.80	f		
Theriault and Goulet [1979][a]	East Montreal Refinery	3	8.48	0.35		x[d]	
Theriault and Provencher [1987]	East Montreal Refinery	7	15.78	0.44	e	x[d]	
Christie [1986]	Australia	9	18.80	0.48	e		
Nakamura [1987]	51 Japanese Refineries	18	19.80	0.91			
Total		1,903	2,469.60	0.77	(p<.00001)		

[a]Note: Blank entries indicate that the observed and expected deaths are not reported by the authors.
[b]Excluded from the calculation of summary SMR.
[c]Only refinery employees are included.
[d]Only male hourly employees with 1 or more years of employment are included.
[e]x = Analysis done.
[f]$p < .05$.
[g]$p < .01$.

significantly low mortality from pancreatic cancer among Chevron employees at the Richmond and El Segundo refineries (SMR = 0.59, $p < .05$). Hanis et al. [1982] reported an SMR of 1.52 ($p = .05$, borderline significance). However, the subsequent Hanis et al. [1985a,b] study found a much reduced SMR of 1.07 ($p = .65$, not significant). No dose-response relationship was demonstrated by any of the studies.

For the entire industry, the pancreatic cancer meta-SMR was 0.95 (336 observed deaths, $p = .32$). The data did not indicate an excess of pancreatic cancer in refinery workers.

Lung Cancer (ICD8, 162, 163)

As indicated in Table VI, most of the studies showed a significant lung cancer deficit. Four of the five industrywide studies showed a significant deficit. The U.S. industrywide study, based on 270 lung cancer deaths, showed an SMR of 0.85 ($p < .05$), significantly less than the expected [Kaplan, 1986]. The two industrywide

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studies in Britain also reported similar results: SMR of 0.78 in refinery workers [Rushton and Alderson, 1981a] and SMR of 0.80 in distribution workers [Rushton and Alderson, 1983], both significant at the .01 level. The Australian registry for the petroleum industry also reported a significant lung cancer deficit (SMR = 0.48). The Japanese industrywide study showed a slight nonsignificant deficit.

Significant lung cancer deficits were also detected in AMOCO refineries [Nelson, 1985], Chevron Richmond and El Segundo refineries [Wong et al., 1986], Texaco refinery and production workers [Divine et al., 1985; Divine and Barron, 1987], and the Shell East Montreal refinery [Thériault and Goulet, 1979].

The Imperial Oil study by Hanis et al. [1979] concluded that there was a significant lung cancer excess among the exposed employees when compared to the nonexposed employees (not shown in Table VI). As commented above, because of the limited job history data, misclassification of exposure was likely. Furthermore, most of the lung cancer cases in that study were office workers, clerks, boiler makers, and construction workers. In some of these occupations, asbestos exposure was likely. Furthermore, when the data were examined by exposure category, the medium exposure group had a lung cancer relative risk (RR) of 0.39, when compared to the nonexposed. This was not consistent with a causal relationship. The most serious evidence against the positive finding in this study is that its lung cancer result was totally inconsistent with the rest of the industry worldwide.

No study has adequate smoking data for a proper analysis incorporating such information. However, in a few studies, some smoking data were available. In the Nelson [1985] study, smoking data were available on 60% of the cohort members, and among those with such information, 69% used tobacco. In the Exxon cohort, smoking information was available on 70% of the employees, among whom 73% smoked cigarettes [Hanis et al., 1985b]. In the Enterline and Henderson [1985] study, smoking data were collected on 71% of the Mobil Torrance cohort, with 65% among them having ever smoked. Van Peenen et al. [1984] reported that 72% of white male refinery hourly employees studied at Standard Oil of Indiana smoked cigarettes, pipes, or cigars. These figures from the above companies, although limited, were quite comparable to the percentage of smokers in the general population. Thus, smoking was not likely a serious confounder when comparing petroleum employee cohorts to the general population.

Summing up all the data on lung cancer, the meta-SMR was calculated to be 0.77. This SMR was extremely stable, with 1,903 observed deaths, and was significant at the .00001 level. Based on the totality of the data, there was a significant lung cancer deficit in petroleum workers.

Skin Cancer (ICD8, 172, 173)

The reported skin cancer mortality in petroleum workers spread over a wide range (Table VII): from a low of 0.24 among the Mobil Paulsboro employees [Morgan and Wong, 1985] to a high of 2.16 in the British industrywide study of refinery employees [Rushton and Alderson, 1981a]. In the Rushston and Alderson study, only melanoma was reported, and 11 of the 14 melanoma deaths came from two of the eight refineries. No dose-response analysis was provided in the study, and no explanation for the excess was offered. In the AMOCO study, the skin cancer SMR of 1.93 (2.01 for white males) was of borderline significance ($p = .05$). Other studies showing a nonsignificant elevation in skin cancer mortality included the Mobil

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TABLE VII. Summary of Mortality From Skin Cancer in Cohort Studies of Refinery and Other Petroleum Employees[a]

Author:year	Facility	Observed deaths	Expected deaths	SMR	Statistical significance	Latency analysis	Duration analysis
Tabershaw Cooper Assc [1974][a]	17 refineries						
Wong [1980][a]	17 refineries						
Kaplan [1986][a]	17 refineries	15	14.05	1.07			
Schottenfeld et al. [1981][a,b]	U.S. refineries	3(m)	3.35	0.89			
Nelson [1985]	10 refineries	11	5.70	1.93			
Wong et al. [1986]	Richmond, El Segundo Refineries	10	10.81	0.92		[d]	[d]
Hanis et al. [1982][a]	Baton Rouge Refinery						
Hanis et al. [1985a]	Baton Rouge, Baytown, Bayway Refineries	9	9.10	0.99			
Wen et al. [1983][c]	Port Arthur Refinery	10	9.53	1.05			
Morgan and Wong [1984]	Beaumont Refinery	7	5.03	1.39		[d]	[d]
Morgan and Wong [1985]	Paulsboro Refinery	1	4.06	0.24		[d]	[d]
Enterline and Henderson [1985]	Torrance Refinery	1(m)[e]	1.02	0.98		[d]	[d]
McCraw et al. [1985]	Wood River Refinery						
Joyner [1983]	Deer Park Refinery						
Divine et al. [1985]	13 refineries & others	14	16.70	0.84			
Divine and Barron [1987]	Production & pipeline	7	9.80	0.72		[d]	[d]
Rushton and Alderson [1981a]	3 UK refineries	14(m)[e]	6.48	2.16	f		
Rushton and Alderson [1983]	UK distribution centers	5	8.52	0.59			
Theriault and Goulet [1979][a]	East Montreal Refinery						
Theriault and Porvencher [1987]	East Montreal Refinery						
Christie [1986]	Australia	4(m)[e]	2.48	1.62			
Nakamura [1987]	51 Japanese refineries						
Total		93	89.23	1.04	(p = .70)		

[a]Note: Blank entries indicate that the observed and expected deaths are not reported by the authors.
[b]Excluded from the calculation of summary SMR.
[c]Only refinery employees are included.
[d]Only male hourly employees with 1 or more years of employment are included.
[d]x = Analysis done.
[e](m) = melanoma only.
[f]p < .01.

Beaumont refinery (SMR = 1.39, 7 observed deaths) and the Australian registry of petroleum workers (SMR = 1.62, 4 observed). In both cases, the numbers of observed deaths were small, and the SMRs were not statistically significant. Furthermore, analyses by length of employment and latency in the Mobil Beaumont study did not find any association between skin cancer and employment [Morgan and Wong, 1984].

On the other hand, skin cancer deficits were reported in the Mobil Paulsboro refinery [Morgan and Wong, 1985], the Texaco refinery and production employees [Divine et al., 1985; Divine and Barron, 1987], and the distribution workers of three companies in Britain [Rushton and Alderson, 1983].

The meta-SMR for skin cancer based on all the eligible studies in the petroleum industry was 1.04 (93 observed deaths and 89.23 expected), with a p-value of .70. Thus, although the results were not always consistent, the overall data indicated that petroleum workers had a similar mortality experience as the general population.

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TABLE VIII. Summary of Mortality From Prostatic Cancer in Cohort Studies of Refinery and Other Petroleum Employees

Author/year	Facility	Observed deaths	Expected deaths	SMR	Statistical significance	Latency analysis	Duration analysis
Tabershaw Cooper Assc. [1974][a]	17 refineries						
Wong [1980][a]	17 refineries						
Kaplan [1986][a,c]	17 refineries	60	58.81	1.02			
Schottenfeld et al. [1981][a,b]	U.S. refineries	5	5.30	0.94			
Nelson [1985]	10 refineries	14	16.20	0.86			
Wong et al. [1986]	Richmond, El Segundo Refineries	34	43.36	0.78		x[d]	x[d]
Hanis et al. [1982][a]	Baton Rouge Refinery	19	28.60	0.66			
Hanis et al. [1985a]	Baton Rouge, Baytown, Bayway Refineries	56	73.30	0.76			
Wen et al. [1983][c]	Port Arthur Refinery	69	59.98	1.15		xx[e]	xx[e]
Morgan and Wong [1984]	Beaumont Refinery	36	32.06	1.12		x[d]	x[d]
Morgan and Wong [1985]	Paulsboro Refinery	28	20.68	1.35		x[d]	x[d]
Enterline and Henderson [1985]	Torrance Refinery	5	4.53	1.10		x[d]	x[d]
McCraw et al. [1985]	Wood River Refinery						
Joyner [1983]	Deer Park Refinery						
Divine et al. [1985]	13 refineries & others	62	73.10	0.85			
Divine and Barron [1987]	Production & pipeline	41	43.70	0.94		x[d]	x[d]
Rushton and Alderson [1981a]	3 UK refineries	47	45.87	1.02			
Rushton and Alderson [1983]	UK distribution centers	53	48.57	1.09			
Theriault and Goulet [1979][a]	East Montreal Refinery						
Theriault and Provencher [1987]	East Montreal Refinery						
Christie [1986]	Australia						
Nakamura [1987]	51 Japanese refineries						
Total		445	461.35	0.96	(p = .45)		

[a]Note: Blank entries indicate that the observed and expected deaths are not reported by the authors.
[b]Excluded from the calculation of summary SMR.
[c]Only refinery employees are included.
[d]Only male hourly employees with 1 or more years of employment are included.
[e]x = Analysis done.
[f]xx = Analysis done for subcohort only in subsequent report (see text).

However, it must be pointed out that the above assessment of skin cancer based on mortality data is limited, since most forms of skin cancer are not fatal.

Prostatic Cancer (ICD8, 185)

Table VIII presents the results of prostatic cancer from the cohort studies of petroleum workers. In most cases, the observed mortality was close to the expected. The highest SMR was observed in the Mobil Paulsboro refinery, with a nonsignificant SMR of 1.35 based on 28 deaths. Detailed analysis showed that the white male employees with 20 years of service at the Paulsboro refinery experienced a significantly elevated SMR of 1.60. However, analysis by work location did not reveal any particular high-risk area.

Two small studies of Methyl ethyl ketone (MEK)-dewaxing employees at refineries have shown a significantly increased rate of prostatic cancer [Enterline, 1978; Wen et al., 1985]. These included the Shell Deer Park refinery (SMR = 9.52, 2 observed deaths, $p < .01$) and the Gulf Port Arthur refinery (SMR = 2.48 for the

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nonwhites based on 7 deaths, $p < .05$; and SMR = 11.49 for those with 20 − years of service and 20–29 years of latency, $p < .05$). However, a similar study of MEK-dewaxing employees at the Shell Haven and Stanlow refineries in Britain [Alderson and Rattan, 1980] did not find any deaths from prostatic cancer, when the expected number was 0.46. Based on these three studies, the meta-SMR for MEK-dewaxing employees was 1.93 ($p < .05$). It should be noted that all three MEK-dewaxing studies were very small.

The meta-SMR for the industry as a whole was 0.96, based on 445 observed deaths ($p = .45$). Thus, petroleum employees as a group had a similar mortality from prostatic cancer as the general population. However, data from some refineries suggested that petroleum employees working at MEK-dewaxing units might experience a higher prostatic cancer risk. At this point, a firm conclusion on the relationship between prostatic cancer and employment at MEK-dewaxing units cannot be made based on the currently available data.

Kidney Cancer (ICD8, 189)

Table IX presents the results of kidney cancer from petroleum cohort mortality studies. Interest in this cancer site was aroused after it was reported [McFarland et al., 1984] that male rats experienced an increase in kidney tumors after chronic exposure to wholly vaporized unleaded gasoline.

The lowest SMR was observed in Texaco production and pipeline workers, with an SMR of 0.35 (5 observed deaths $p < .05$). However, production workers have limited contact with downstream gasoline, and, thus, their mortality experience might not be directly relevant. The Chevron refinery study and the three Mobil refinery studies all reported slight deficits in kidney cancer mortality with SMRs ranging from a low of 0.59 (1 death) to a high of 0.81 (12 deaths).

Mortality excess from kidney cancer was observed in both Exxon and Gulf employees. For the three Exxon refineries at Baton Rouge, Baytown, and Bayway, the SMR for kidney was 1.43 (22 deaths, $p = .09$). The excess came from those hired before 1956, the SMR being 1.47 (22 deaths, $p = .07$). Unfortunately, no length of employment analysis was done. Wen et al. [1984b] reported some detailed analyses of kidney cancer based on the Gulf Port Arthur study. Overall, the Gulf Port Arthur cohort experienced a nonsignificant SMR of 1.23 based on 22 deaths with a p-value of .33 [Wen et al., 1984b]. When the data were analyzed by length of employment, a weak upward trend was found. For those who worked for 9, 10–20, and ≥ 20 years, the SMRs were 0.93, 1.25, and 1.38, respectively. A subsequent nested case-control study detected several areas with nonsignificant increase in kidney cancer. The Japanese industrywide study did not report kidney cancer per se. However, for urinary tract cancer, the Japanese refinery workers experienced a borderline significant excess ($p = .05$), with 7 observed deaths and an SMR of 2.05 [Nakamura, 1987].

As far as downstream gasoline is concerned, the more appropriate group to study is the distribution or marketing employees. In the British distribution employees, a nonsignificant excess from kidney cancer of 1.21 (based on 23 deaths, $p = .37$) was reported [Rushton and Alderson, 1983]. However, detailed analysis (in the original report to the sponsor but not reported in the published article) showed that drivers, who had the highest exposure to gasoline, experienced an SMR of 1.71 (12

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TABLE IX. Summary of Mortality From Kidney Cancer in Cohort Studies of Refinery and Other Petroleum Employees[a]

Author/year	Facility	Observed deaths	Expected deaths	SMR	Statistical significance	Latency analysis	Duration analysis
Tabershaw Cooper assc. (1974)[a]	17 refineries						
Wong (1980)[a]	17 refineries						
Kaplan (1986)[a]	17 refineries	15	22.09	0.68			
Schottenfeld et al. (1981)[a,b]	U.S. refineries						
Nelson (1985)	10 refineries	9	8.40	1.07			
Wong et al. (1986)	Richmond, El Segundo Refineries	12	14.82	0.81		x[d]	x[d]
Hanis et al. (1982)[a]	Baton Rouge Refinery	9	5.80	1.55			
Hanis et al. (1985a)	Baton Rouge, Baytown, Bayway Refineries	22	15.40	1.43			
Wen et al. (1983)[c]	Port Arthur Refinery	19	14.87	1.28		xx[e]	xx[e]
Morgan and Wong (1984)	Beaumont Refinery	6	7.90	0.75		x[d]	x[d]
Morgan and Wong (1985)	Paulsboro Refinery	4	6.17	0.64		x[d]	x[d]
Enterline and Henderson (1985)	Torrance Refinery	1	1.69	0.59		x[d]	x[d]
McCraw et al. (1985)	Wood River Refinery						
Joyner (1983)	Deer Park Refinery						
Divine et al. (1985)	13 refineries & others	24	25.10	0.96			
Divine and Barron (1987)	Production & pipeline	5	14.10	0.35	f	x[d]	x[d]
Rushton and Alderson (1981a)	8 UK refineries	22	21.74	1.01			
Rushton and Alderson (1983)	UK distribution centers	23	19.05	1.21			
Theriault and Goulet (1979)[a]	East Montreal Refinery						
Theriault and Provencher (1987)	East Montreal Refinery						
Christie (1986)	Australia						
Nakamura (1987)	51 Japanese refineries						
Total		147	149.24	0.98	(p = .85)		

[a]Note: Blank entries indicate that the observed and expected deaths are not reported by the authors.
[b]Excluded from the calculation of summary SMR.
[c]Only refinery employees are included.
[d]Only male hourly employees with 1 or more years of employment are included.
[e]x = Analysis done.
[f]xx = Analysis done in subsequent report (see text).
[g]$p < .05$.

deaths, $p = .05$, borderline significance). A significant excess was detected among men aged 55–64 years (SMR = 1.89, $p < .05$).

For the industry as a whole, the kidney cancer meta-SMR was 0.98, based on 147 deaths. The data were somewhat conflicting. On the one hand, production workers at Texaco experienced a significantly low kidney cancer mortality. On the other hand, drivers among British distribution workers experienced a borderline significant increase. The results from refinery studies ranged from nonsignificant deficits to nonsignificant excesses. Additional data, particularly from those exposed to downstream gasoline, are needed to resolve this issue.

Brain and Central Nervous System (CNS) Cancer (ICD8, 191–192)

Several studies of petroleum employees showed some nonsignificant excess of brain and CNS cancer (Table X). The API-MSKCC registry showed an SMR of 1.63 ($p = .16$, not significant). Among the Gulf nonwhite males [Wen et al., 1983], a

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TABLE X. Summary of Mortality From Brain Cancer in Cohort Studies of Refinery and Other Petroleum Employees[a]

Author/year	Facility	Observed deaths	Expected deaths	SMR	Statistical significance	Latency analysis	Duration analysis
Tabershaw Cooper Assc. [1974][a]	17 refineries						
Wong [1980][a]	17 refineries	8	11.29	0.71			
Kaplan [1986][a, c]	17 refineries	22	24.63	0.89			
Schottenfeld et al. [1981][a, b]		8	4.90	1.63			
Nelson [1985]	10 refineries	8	9.60	0.83			
Wong et al. [1986]	Richmond, El Segundo Refineries	22	17.48	1.25		x[d]	x[d]
Hanis et al. [1982][a]	Baton Rouge Refinery	5	4.90	1.02			
Hanis et al. [1985a]	Baton Rouge, Baytown, Bayway Refineries	15	13.00	1.15			
Wen et al. [1983][c]	Port Arthur Refinery	23	22.85	1.01		xx[e]	xx[e]
Morgan and Wong [1984]	Beaumont Refinery	9	8.26	1.09		x[d]	x[d]
Morgan and Wong [1985]	Paulsboro Refinery	7	6.64	1.05		x[d]	x[d]
Enterline and Henderson [1985]	Torrance Refinery	3	2.09	1.43		x[d]	x[d]
McCraw et al. [1985]	Wood River Refinery						
Joyner [1983]	Deer Park Refinery						
Divine et al. [1985]	13 refineries & others	31	28.00	1.11			
Divine and Barron [1987]	Production & pipeline	11	15.90	0.69		x[d]	x[d]
Rushton and Alderson [1981a]	8 UK refineries	36	44.77	0.80			
Rushton and Alderson [1983]	UK distribution centers	39	36.54	1.07			
Thériault and Goulet [1979][a]	East Montreal Refinery	3	0.77	3.89		x[d]	
Thériault and Provencher [1987]	East Montreal Refinery	4	1.87	2.13		x[d]	
Christie [1986]	Australia	2	2.70	0.74			
Nakamura [1987]	51 Japanese Refineries						
Total		210	209.7	1.00	(p = .99)		

[a]Note: Blank entries indicate that the observed and expected deaths are not reported by the authors.
[b]Excluded from the calculation of summary SMR.
[c]Only refinery employees are included.
[d]Only male hourly employees with 1 or more years of employment are included.
[e]x = Analysis done.
[f]xx = Analysis done in subsequent report (see text).

brain cancer SMR of 1.63 was detected (not significant). In the Mobil Torrance refinery, an SMR of 1.43 based on 3 deaths was reported ($p = .50$, not significant). In Canada, the Shell Canada East Montreal refinery employees had an SMR of 2.13 ($p = .12$, not significant). All these studies were based on very small numbers (Table X).

Based on the PMR study of the Gulf and Texaco Port Arthur refineries, Thomas et al. [1980] reported higher than expected brain cancer mortality among the refinery employees. A subsequent PMR study of brain cancer of the Gulf and Texaco Port Arthur and the Mobil Beaumont refineries also reported elevated brain cancer PMRs [Thomas et al., 1982b]. Other subsequent studies addressing the issue of brain cancer and benign brain tumors were also reported [Wong, 1980; Wen et al., 1982]. Wong [1980] concluded that there was no brain cancer excess in the TCA industrywide study (SMR = 0.71 based on 8 deaths), which was confirmed by a later update of the study (SMR = 0.89 based on 22 deaths) [Kaplan, 1986]. Wen et al. [1982] analyzed both malignant and benign brain tumors in the Gulf Port Arthur refinery employees.

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Although the SMR of 0.97 (30 deaths) for the entire refinery was similar to the expected, those with 20 or more years of employment experienced an SMR of 1.43 ($p = .10$, not significant), which was more than twice that for those with less than 10 years of service (SMR = 0.59). A subsequent case-control study by Thomas et al. [1984] on three Texas refineries including the Gulf Port Arthur plant did not find any work category associated with brain tumor mortality.

Another approach to evaluate the issue of brain cancer in petroleum workers is to examine the data for any dose-response relationship. A few studies provided analyses by length of employment. No trend was found for brain cancer with respect to length of service in the Chevron Richmond and El Segundo refineries [Wong et al., 1986], the Mobil Beaumont and Paulsboro refineries [Morgan and Wong, 1984, 1985], and the laboratory workers at the Texaco refineries [Divine and Barron, 1987]. Thus, analysis by length of service did not support a causal association between refinery employment and brain cancer.

Brain cancer is a highly fatal disease. Little is known about its etiology, and no preventive behavior or medical intervention has demonstrated any significant benefits. As such, brain cancer in industrial groups is not expected to be influenced by the healthy worker effect, and the corresponding SMR, in the absence of any occupational carcinogens, is expected to be close to 1.

Overall, the petroleum workers experienced an identical brain cancer mortality as the general population (meta-SMR = 1.00, $p = .99$). Although some studies showed nonsignificant excesses from brain cancer, these studies were small. It has been demonstrated that industrial workers were more likely to have an overdiagnosis of brain tumors as a result of more complete medical evaluation, "diagnostic sensitivity bias" [Greenwald et al., 1981]. It has also been demonstrated that socioeconomic class can also influence diagnostic sensitivity for brain cancer [Levine, 1985]. Further investigations in this direction on petroleum workers are needed.

Lymphatic and Hematopoietic Cancer (ICD8, 200–209)

Of the studies listed in Table XI, a few studies showed modest increases in lymphatic and hematopoietic cancer. A significant excess was found in Mobil Beaumont refinery employees (SMR = 1.47, 47 deaths, $p < .05$). Similar excesses, although not statistically significant, were also found in the Shell Wood River refinery and the participants in the Australian registry. The AMOCO study showed a significant deficit (SMR = 0.60, $p < .05$). Other studies based on a reasonable number of deaths indicated that the mortality was similar to the expected.

Several studies with length of service analysis indicated an increased mortality from lymphatic and hematopoietic cancer with increasing length of service. These studies included the Chevron Richmond and El Segundo refineries [Wong et al., 1986], and the Mobil Beaumont refinery [Morgan and Wong, 1984].

On an industry basis, the meta-SMR was 1.03 (based on 460 deaths, $p = .58$). Individual study results were not consistent. Both significantly high and low SMRs were reported. It would, perhaps, be more informative to examine the specific subgroups within the broad category of lymphatic and hematopoietic cancer.

Lymphosarcoma and Recticulosarcoma (ICD8, 200)

For lymphosarcoma and recticulosarcoma, three cohorts with reasonable numbers of deaths reported nonsignificant excesses (Table XII). In the Chevron study, the

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TABLE XI. Summary of Mortality From Lymphopoietic Cancer in Cohort Studies of Refinery and Other Petroleum Employees[a]

Author/year	Facility	Observed deaths	Expected deaths	SMR	Statistical significance	Latency analysis	Duration analysis
Tabershaw Cooper Assc. [1974][a]	17 refineries						
Wong [1980][a]	17 refineries						
Kaplan [1986][a]	17 refineries	98	82.50	1.07			
Schottenfeld et al. [1981][a,b]	U.S. refineries						
Nelson [1985]	10 refineries	17	28.50	0.60	c		
Wong et al. [1986]	Richmond, El Segundo Refineries	64	60.97	1.05		x[d]	x[d]
Hanis et al. [1982][a]	Baton Rouge Refinery	25	23.00	1.09			
Hanis et al. [1985a]	Baton Rouge, Baytown, Bayway Refineries	55	61.80	0.89			
Wen et al. [1983][c]	Port Arthur Refinery	62	58.62	1.06			
Morgan and Wong [1984]	Beaumont Refinery	47	31.89	1.47	c	x[d]	x[d]
Morgan and Wong [1985]	Paulsboro Refinery	23	24.52	0.93		x[d]	x[d]
Enterline and Henderson [1985]	Torrance Refinery	5	6.63	0.75		x[d]	x[d]
McCraw et al. [1985]	Wood River Refinery	22	15.20	1.44			
Joyner [1983]	Deer Park Refinery						
Divine et al. [1985]	13 refineries & others	106	96.70	1.10			
Divine and Barron [1987]	Production & pipeline	48	54.60	0.88		x[d]	x[d]
Rushton and Alderson [1981a]	8 UK refineries						
Rushton and Alderson [1983]	UK distribution centers						
Theriault and Gouiet [1979][a]	East Montreal Refinery	3	2.36	1.27		x[d]	
Theriault and Provencher [1987]	East Montreal Refinery	3	4.44	0.67		x[d]	
Christie [1986]	Australia	9	4.84	1.65			
Nakamura [1987]	51 Japanese Refineries						
Total		460	448.71	1.03	(p = .58)		

*Note: Blank entries indicate that the observed and expected deaths are not reported by the authors.
[a]Excluded from the calculation of summary SMR.
[b]Only refinery employees are included.
[c]Only male hourly employees with 1 or more years of employment are included.
[d]x = Analysis done.
[e]$p < .05$.

SMR was 1.26. Length of employment indicated that those with 15 years of employment had an SMR of 1.62 (14 deaths, $p = .07$, not significant). In 1947, the recommended benzene standard [8-hour Time-Weighted Average (TWA)] in the United States was lowered from 100 ppm to 50 ppm, and in 1948, it was further lowered to 35 ppm. To determine the impact of this significant reduction in the benzene standard, analysis by hire date was done in the Chevron study. Among those hired before 1948 at the Richmond refinery, the SMR was 1.87 (13 deaths, $p = .05$), whereas there was no excess among those hired after 1948. Although this analysis by hire date was somewhat confounded by latency, an adequate latency (some with over 30 years) was achieved by those hired after 1948. Thus, there was some suggestive evidence that historical benzene exposure might be related to an increase in lymphosarcoma and recticulosarcoma. At the Mobil Beaumont refinery, the analysis by length of service did not show any pattern, but the analysis by latency showed an upward trend. The Exxon cohort showed a slight, nonsignificant excess.

All other studies with a reasonable number of deaths showed a deficit from this

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TABLE XII. Summary of Mortality From Lymphosarcoma in Cohort Studies of Refinery and Other Petroleum Employees*

Author/year	Facility	Observed deaths	Expected deaths	SMR	Statistical significance	Latency analysis	Duration analysis
Tabersnaw Cooper Assc [1974][a]	17 refineries						
Wong [1980][a]	17 refineries						
Kaplan [1986][a]	17 refineries	16	17.78	0.90			
Schottenfeld et al. [1981][a,b]	U.S. refineries						
Nelson [1985]	10 refineries						
Wong et al. [1986]	Richmond, El Segundo Refineries	17	13.43	1.26		x[d]	x[d]
Hanis et al. [1982][a]	Baton Rouge Refinery	5	4.20	1.19			
Hanis et al. [1985a]	Baton Rouge, Baytown, Bayway Refineries	13	11.40	1.14			
Wen et al. [1983][c]	Port Arthur Refinery	2	11.69	0.17	e		
Morgan and Wong [1984]	Beaumont Refinery	10	6.81	1.46		x[d]	x[d]
Morgan and Wong [1985]	Paulsboro Refinery	3	5.36	0.55		x[d]	x[d]
Enterline and Henderson [1985]	Torrance Refinery	1	1.55	0.64		x[d]	x[d]
McCraw et al. [1985]	Wood River Refinery	0	2.80	0.00			
Joyner [1983]	Deer Park Refinery						
Divine et al. [1985]	13 refineries & others	20	22.20	0.90			
Divine and Barron [1987]	Production & pipeline	7	11.80	0.59		x[d]	x[d]
Rushton and Alderson [1981a]	3 UK refineries	16	16.26	0.98			
Rushton and Alderson [1983]	UK distribution centers	7	8.05	0.87			
Theriault and Goulet [1979][a]	East Montreal Refinery						
Theriault and Provencher [1987]	East Montreal Refinery						
Christie [1986]	Australia	1	0.40	2.48			
Nakamura [1987]	51 Japanese Refineries						
Total		97	111.75	0.87	(p = .16)		

*Note: Blank entries indicate that the observed and expected deaths are not reported by the authors.
[a]Excluded from the calculation of summary SMR.
[b]Only refinery employees are included.
[c]Only male hourly employees with 1 or more years of employment are included.
[d]x = Analysis done.
[e]p < .01.

cause of death. The lowest SMR was observed in white male employees at the Gulf Port Arthur refinery, 1 observed vs. 10 expected. None of the studies reporting a deficit based on a reasonable number of deaths made any attempt to analyze the data by length of employment.

For the industry as a group, the meta-SMR was 0.87 with a p-value of .16. Although the Chevron data were consistent with an increase, the increase was modest and was associated with historical exposure. The weight of the evidence favors a conclusion of a similar or slightly lower mortality risk from this cause for petroleum workers when compared to the general population.

Leukemia (ICD8, 204–207)

Because of potential exposure to benzene in the petroleum industry, leukemia is perhaps one of the most serious concerns as well as one of the most studied causes. In addition to analysis in the cohort studies, some case-control studies within the

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TABLE XIII. Summary of Mortality From Leukemia in Cohort Studies of Refinery and Other Petroleum Employees[a]

Author/year	Facility	Observed deaths	Expected deaths	SMR	Statistical significance	Latency analysis	Duration analysis
Tabersnaw Cooper Assc. [1974][a]	17 refineries	10	12.18	0.82			
Wong [1980][a]	17 refineries						
Kaplan [1986][a]	17 refineries	32	31.68	1.01			
Schottenfeld et al. [1981][a,b]	U.S. refineries	4	5.98	0.66			
Nelson [1985]	10 refineries	4	9.70	0.41	f		
Wong et al. [1986]	Richmond, El Segundo Refineries	22	24.92	0.88		x[d]	x[d]
Hanis et al. [1982][a]	Baton Rouge Refinery	9	9.30	0.97			
Hanis et al. [1985a]	Baton Rouge, Baytown, Bayway Refineries	20	25.90	0.77			
Wen et al. [1983][c]	Port Arthur Refinery	33	25.08	1.32		xx[e]	xx[e]
Morgan and Wong [1984]	Beaumont Refinery	23	13.31	1.72	f	x[d]	x[d]
Morgan and Wong [1985]	Paulsboro Refinery	10	10.28	0.97		x[d]	x[d]
Enterline and Henderson [1985]	Torrance Refinery	2	2.54	0.78		x[d]	x[d]
McCraw et al. [1985]	Wood River Refinery	14	6.60	2.13	f		
Joyner [1983]	Deer Park Refinery	6	2.60	2.30	f		
Divine et al. [1985]	13 refineries & others	48	40.70	1.18			
Divine and Barron [1987]	Production & pipeline	25	22.70	1.10		x[d]	x[d]
Rushton and Alderson [1981a]	8 UK refineries	30	31.96	0.94			xx[e]
Rushton and Alderson [1983]	UK distribution centers	28	26.82	1.04			
Theriault and Goulet [1979][a]	East Montreal Refinery						
Theriault and Provencher [1987]	East Montreal Refinery						
Christie [1986]	Australia	5	1.93	2.59			
Nakamura [1987]	51 Japanese Refineries	9	8.5	1.06			
Total		279	253.54	1.10	(p = .10)		

[a]Note: Blank entries indicate that the observed and expected deaths are not reported by the authors.
[a]Excluded from the calculation of summary SMR.
[b]Only refinery employees are included.
[c]Only male hourly employees with 1 or more years of employment are included.
[d]x = Analysis done.
[e]xx = Analysis done in subsequent report (see text).
[f]$p < .05$.

petroleum industry have also been done. Table XIII shows the results of the cohort studies.

Most of the studies reported either a similar or a higher leukemia mortality experience. Only the AMOCO study reported a significant deficit in leukemia. The number of deaths involved was only 4. This result was inconsistent with the rest of the industry.

Several studies reported significant leukemia excesses. Although the original Gulf Port Arthur refinery study, [Wen et al., 1983] found a nonsignificant leukemia excess (SMR = 1.32, Table XIII), an unpublished update of the study through the end of 1983 [Wen et al., 1984c] showed a significant leukemia excess among employees with 20 or more years of service (SMR = 1.63, $p < .01$). The excess came mainly from lymphocytic and other unspecified cell types. Furthermore, an upward trend was found by length of service. According to the updated data, of the 43 leukemias at Gulf, 28 had a latency of 30 or more years.

The Mobil Beaumont refinery showed a significant leukemia SMR of 1.72 for

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the entire cohort (23 deaths, $p < .05$). Analysis by length of employment among the white males detected a significant SMR of 2.35 for those with 30 or more years of service. Similar analysis showed a significant SMR of 2.14 in white males with a latency of 20–39 years. Different cell types were observed.

Elevated leukemia mortality was found at the Shell refineries at Wood River and Deer Park. At Wood River, 14 leukemias were seen when only 6.6 were expected [McCraw et al., 1985]; the SMR was 2.13 ($p < .05$). The excess was associated predominantly with acute myelogenous leukemia (SMR = 3.94, $p < .01$); however, leukemias of other cell types were also observed. A similar significant excess was also found at the Shell Deer Park refinery [Joyner, 1983]. Six leukemia deaths were identified, producing an SMR of 2.30 ($p < .05$). Three of the leukemias were acute myelogenous leukemia, and the corresponding SMR was 3.60 ($p < .05$). However, a subsequent nested case-control study failed to identify any specific locations or jobs responsible for the excess [Austin et al., 1986].

The Australian registry, even though the follow-up was very short, detected an increase in leukemia mortality (5 observed, SMR = 2.59, $p < .05$).

Although the industrywide refinery study [Rushton and Alderson, 1981a] in Britain found a leukemia mortality for the entire cohort similar to that for the general population, a subsequent case-control study [Rushton and Alderson, 1981b] found a more than threefold risk among those with either medium or high exposure when compared to those with low benzene exposure.

Although the industry overall experienced only a small excess in leukemia (meta-SMR = 1.10, $p = .10$), there is suggestive evidence that some small groups within the industry may have had significantly elevated leukemia risk. This conclusion is based on several considerations: the significant excesses observed for the entire refineries in several studies [Morgan and Wong, 1984; McCraw et al., 1985]; increased risks with increasing length of service [Wen et al., 1983; Morgan and Wong, 1984]; and case-control studies within the industry [Rushton and Alderson, 1981b]. However, several issues remain unresolved at this time.

First, high-risk groups have not been identified, and only a few studies provided job- or area-specific analyses. Most of the leukemia cases in the petroleum industry were not found among those who worked on benzene units directly [Tsai et al., 1983; McCraw et al., 1985]. Large case-control studies with detailed employment and exposure data are needed to identify high-risk groups. Second, except for the two Shell refineries, most refinery studies reported a variety of cell types, not limited to acute myelogenous leukemia alone. The issue of whether benzene or other petroleum hydrocarbons can affect only acute myelogenous leukemia or other cell types as well remains unresolved. Third, diagnostic specificity (or lack of) for lymphatic and hematopoietic diseases on death certificates, particularly on older death certificates, may result in inaccuracy of underlying cause of death classification. This misclassification may confound site-specific analyses. Fourth, latency in these leukemia cases was of the order of 20–30 years, different from the short latency reported for benzene-related leukemias in the early literature. By comparison, benzene exposure at refineries is much lower than those reported earlier (e.g., shoemakers in Turkey) [Aksoy and Erdem, 1978]. The data suggest that latency is inversely related to intensity of exposure. This hypothesis needs verification. Fifth, it is not clear at this point whether benzene was the only responsible agent or if other chemicals were also involved.

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TABLE XIV. Summary of Mortality From Other Lymphatic Tissue Cancer in Cohort Studies of Refinery and Other Petroleum Employees[a]

Author/year	Facility	Observed deaths	Expected deaths	SMR	Statistical significance	Latency analysis	Duration analysis
Tabershaw Cooper Assc. [1974][a]	17 refineries						
Wong [1980][a]	17 refineries						
Kaplan [1986][a]	17 refineries	30	22.82	1.31			
Schottenfeld et al. [1981][a,b]	U.S. refineries						
Nelson [1985]	10 refineries						
Wong et al. [1986]	Richmond, El Segundo Refineries	20	14.12	1.41		[c,d]	[c,d]
Harris et al. [1982][a]	Baton Rouge Refinery	7	7.20	0.97			
Harris et al. [1985a]	Baton Rouge, Baytown, Bayway Refineries	15	18.60	0.81			
Wen et al. [1983][c]	Port Arthur Refinery	14	13.23	1.05			
Morgan and Wong [1984]	Beaumont Refinery	12	7.62	1.57		[c,d]	[c,d]
Morgan and Wong [1985]	Paulsboro Refinery	8	5.66	1.41		[c,d]	[c,d]
Enterline and Henderson [1985]	Torrance Refinery	2	1.96	1.02		[c,d]	[c,d]
McCraw et al. [1985]	Wood River Refinery	6	4.80	1.26			
Joyner [1983]	Deer Park Refinery						
Divine et al. [1985]	13 refineries & others	25	21.80	1.15			
Divine and Barron [1987]	Production & pipeline	12	13.50	0.89		[c,d]	[c,d]
Rushton and Alderson [1981a]	8 UK refineries						
Rushton and Alderson [1983]	UK distribution centers	6	3.63	1.65			
Theriault and Goulet [1979][a]	East Montreal Refinery						
Theriault and Provencher [1987]	East Montreal Refinery						
Christie [1986]	Australia	2	1.47	1.36			
Nakamura [1987]	51 Japanese refineries						
Total		122	106.39	1.15	(p = .13)		

[a]Note: Blank entries indicate that the observed and expected deaths are not reported by the authors.
[b]Excluded from the calculation of summary SMR.
[c]Only refinery employees are included.
[d]Only male hourly employees with 1 or more years of employment are included.
[e]x = Analysis done.

Cancer of the Other Lymphatic Tissue (ICD8, 202, 203, and 208)

Table XIV shows the SMRs for cancer of other lymphatic tissue from the eligible cohort studies. For most studies, the SMR was slightly above the norm. These included the API industrywide study [Kaplan, 1986], the Chevron refineries [Wong et al., 1986], the Mobil refineries at Beaumont and Paulsboro [Morgan and Wong, 1984, 1985], the Shell Wood River refinery [McCraw et al., 1985], and the British distribution workers [Rushton and Alderson, 1983].

Only two studies showed an SMR less than 1: 0.81 for the three Exxon refineries and 0.89 for the Texaco production workers. As stated earlier, the exposure of production workers might not be similar to the refinery workers. Overall, the meta-SMR was 1.15 ($p = .13$). Although the excess is not statistically significant, several points need to be addressed.

In regard to the relationship between "cancer of the other lymphatic tissue" and leukemia, recent immunologic studies have shown that there are stem cells that appear to have the capacity to develop into the following different cell lines: T-cell lymphocytes, plasma cells, granulocytic series cells, erythrocytes, and monocytes

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TABLE XV. Power Analysis by Cancer Site*

Cancer site	Observed deaths	Expected deaths	95% CI			p-value	MIN SMR
			SMR	LL	UL		
All	6,405	7,525.29	0.85	0.83	0.87	< .00001	1.03
Digestive	947	1,174.86	0.81	0.76	0.86	< .00001	1.07
Stomach	585	659.95	0.89	0.82	0.96	< .005	1.10
Pancreatic	336	354.83	0.95	0.85	1.05	= .32	1.14
Lung	1,903	2,469.60	0.77	0.74	0.81	< .00001	1.05
Skin	93	89.23	1.04	0.84	1.28	= .70	1.28
Prostatic	445	461.35	0.96	0.87	1.05	= .45	1.12
Kidney	147	149.24	0.98	0.83	1.15	= .85	1.21
Brain	210	209.70	1.00	0.87	1.15	= .99	1.18
Lymphopoietic	460	448.71	1.03	0.94	1.13	= .58	1.12
Lymphosarcoma	97	111.75	0.87	0.71	1.06	= .16	1.25
Leukemia	279	253.54	1.10	0.97	1.23	= .10	1.16
Other lymphatic tissue	122	106.39	1.15	0.95	1.38	= .13	1.25

*95% CI = confidence interval (upper and lower limits [LL, UL]); MIN SMR = minimum SMR detectable at .05 level with 80% power.

[Minowada et al., 1981]. Further work by Bakhshi et al. [1983] demonstrates that the major clone in chronic myelocytic leukemia involves cells capable of lymphocytic, granulocytic, and erythrocytic differentiation and has led to the conclusion that a transformation event occurs at a very early multipotent stem cell level.

Because this ICD group consists of several lymphatic and hematopoietic cancers, little attention has been focused on this category. Because of the diagnostic overlap, the natural course of various lymphatic cancers [Jaffe and Berard, 1978], and the multipotent stem cell theory [Minowada et al., 1981; Bakhshi et al., 1983; Kersey, 1983], cancer of other lymphatic tissue should be combined with other lymphatic and hematopoietic cancers for analysis [Wong, 1987; Heath, 1982; Decouflé et al., 1983]. A thorough examination of the industry data in this direction will help to resolve this issue.

CONCLUSIONS

Based on this review of the pertinent epidemiologic studies in the petroleum industry, we conclude that employees in this industry with potential exposure to petroleum products including gasoline-like hydrocarbons are not at increased risk for most cancers examined. The statistical power of the combined data from these epidemiologic studies in detecting a modest risk in most cancers is quite high (Table XV). In fact, the review indicates that these employees experienced a significantly lower mortality than the general population from the following cancers: all sites combined, digestive system, stomach, and lung.

For skin cancer and brain cancer, the results from various studies were not always consistent. However, the overall data indicated that the mortality experience for these two cancers of petroleum employees was similar to that in the general population.

For prostatic cancer and kidney cancer, the employees in the petroleum industry as a whole experienced a similar risk as the general population. However, there are

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data indicating that certain small groups within the industry might have an elevated risk. For prostatic cancer, employees at the MEK-dewaxing units may be at higher risk, but the numbers in these studies were very small, and the results were not replicated in a subsequent study. For kidney cancer, one study indicated that gasoline truck drivers were at higher risk. Additional studies of these sites that include exposure information are needed before any relevance to hydrocarbon exposure can be determined.

The review supports the conclusion that some subgroups of petroleum employees, particularly those with more than 20 years of service and employed before the 1940s in the petroleum industry, may have been at increased risk of leukemia. This conclusion is based on the fact that several studies of refinery workers showed a significant excess, on the consistency of the data, on the positive trend with increasing length of employment and latency, and on the results of detailed case-control studies within the industry. Unfortunately, accurate historical exposure data are lacking. In most refineries, industrial hygiene-monitoring data were not been routinely collected until the mid-1970s, whereas relevant exposures in these cohort studies occurred much earlier. A risk assessment by quantitative exposure data cannot be made based on the currently available data. An industrywide case-control study of leukemia, with a strong focus on historical exposure data, would be helpful in such a risk assessment. Furthermore, there is some indication that mortality from cancer of other lymphatic tissue might also be elevated. Owing to the reasons provided earlier, this broad ICD category should be given more attention in the future.

REFERENCES

Aksoy M, Erdem S (1978): Follow-up study on the mortality and the development of leukemia in 44 pancytopenic patients with chronic exposure to benzene. Blood 52:285–292.

Alderson MR, Rattan NS (1980): Mortality of workers in an isopropyl alcohol plant and two MEK dewaxing plants. Br J Ind Med 37:85–89.

Austin H, Cole P, McCraw DS (1986): A case-control study of leukemia at an oil refinery. J Occup Med 28:1169–1173.

Baird VC (1967): Effects of atmospheric contamination on cancer mortality in petroleum refinery employees. J Occup Med 9:415–420.

Bakhshi A, Minowada J, Arnold A, Cossman J, Jensen JP, Wheng-Peng J, Waldmann TA, Korsmeyer SJ (1983): Lymphoid blast crises of chronic myelogenous leukemia represent stages in the development of B-cell precursors. N Engl J Med 309:826–831.

Christie D (1987): Health Watch, The Australian Petroleum Industry Health Surveillance Programme, Sixth Annual Report, 1986.

Day NE (1985): Statistical considerations. In Wald NJ, and Doll R (eds.): "Interpretation of Negative Epidemiologic Evidence for Carcinogenicity." International Agency for Research on Cancer Scientific Publication No. 65, pp 13–27.

DeCouflé P, Blattner WA, Blair A (1983): Mortality among chemical workers exposed to benzene and other agents. Environ Res 30:16–25.

Divine BJ, Barron V (1986): Texaco mortality study: II. Patterns of mortality among white males by specific job groups. Am J Ind Med 10:371–381.

Divine BJ, Barron V (1987): Texaco mortality study: III. A cohort study of producing and pipeline workers. Am J Ind Med 11:189–202.

Divine BJ, Barron V, Kaplan SD (1985): Texaco mortality study: I. Mortality among white male refinery, petrochemical, and research workers. J Occup Med 27:445–447.

Enterline PE (1978): Mortality among workers from Shell Oil Company's lubricants' dewaxing unit at Deer Park, Texas. Report submitted to Shell Oil Company.

Enterline PE, Henderson V (1985): A report on the mortality experience of workers from a petroleum refinery at Torrance, California. Report submitted to the Mobil Oil Corporation.

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Environmental Protection Agency (1987): "Evaluation of the Carcinogenicity of Unleaded Gasoline." Washington DC. United States Environmental Protection Agency.

Greenwald P, Friedlander BR, Lawrence CE, Hearne T, Earle K (1981): Diagnostic sensitivity bias—an epidemiologic explanation for an apparent brain tumor excess. J Occup Med 23:690–694.

Hanis NM, Stavraky KM, Fowler JL (1979): Cancer mortality in refinery workers. J Occup Med 21:167–174.

Hanis NM, Holmes TM, Shallenberger LG, Jones KE (1982): Epidemiologic study of refinery and chemical plant workers. J Occup Med 24:203–212.

Hanis NM, Shallenberger LG, Donaleski DL, Sales EA (1985a): A retrospective mortality study of workers in three major U.S. refineries and chemical plants. Part I: Comparisons with U.S. population. J Occup Med 27:283–292.

Hanis NM, Shallenberger LG, Donaleski DL, Sales EA (1985b): A retrospective mortality study of workers in three major U.S. refineries and chemical plants. Part II: Internal comparisons by geographic site, occupation, and smoking history. J Occup Med 27:361–369.

Harrington JM (1987): Health experience of workers in the petroleum manufacturing and distribution industry: A review of the literature. Am J Ind Med 12:475–497.

Heath CW (1982): Leukemia. In Schottenfeld D, Fraumeni JF, (eds): "Cancer Epidemiology and Prevention." Philadelphia: WB Saunders Company, pp 728–738.

Hill AB (1965): The environment and health: Association or causation. Proc R Soc Med 58:295–300.

Howe GR, Burch JD, Miller AB, Cook GM, Esteve J, Morrison B, Gordon P, Chambers LW, Fodor G, Winsor GM (1980): Tobacco use, occupation, coffee, various nutrients, and bladder cancer. JNCI 64:701–713.

Jaffe ES, Berard CW (1978): Lymphoblastic lymphoma, a term rekindled with new precision. Ann Intern Med 89:415, 416.

Joyner RE (1983): Letter to Dr. J. Donald Millar, Director of National Institute for Occupational Safety and Health, Dated July 28, 1983.

Kaplan SD (1986): Update of a mortality study of workers in petrochemical refineries. J Occup Med 28:514–516.

Kersey JH (1983): Chronic myelocytic (multipotent-stem-cell) leukemia. N Engl J Med 309:851, 852.

Levine RJ (1985): Letter to the editor. Environ Health Perspectives 62:465, 466.

Lin RS, Kessler II (1981): A multifactorial model for pancreatic cancer in man: Epidemiologic evidence. JAMA 245:147–152.

MacFarland HN, Ulrich CE, Holdsworth CE, Kitchen DN, Halliwell WH, Blum SC (1984): A chronic inhalation study with unleaded gasoline vapor. J Am Coll Toxicol 3:231–248.

Matanoski GM, Elliott EA (1981): Bladder cancer epidemiology. Epidemiol Rev 3:203–229.

McCraw DS, Joyner RE, Cole P (1985): Excess leukemia in a refinery population. J Occup Med 27:220–222.

McLaughlin JK, Mandel JS, Blot WJ, Schuman LM, Mehl ES, Fraumeni JF, Jr (1984): A population-based case-control study of renal cell carcinoma. JNCI 72:275–284.

McLaughlin JK, Blot WJ, Mehl ES, Stewart PA, Venable FS, Fraumeni Jr JF (1985): Petroleum-related employment and renal cell cancer. J Occup Med 27:672–674.

Minowada J, Koshiba H, Sagawa K, Kubonishi I, Lok MS, Tatsumi E, Han T, Srivastava BI, Ohnuma T (1981): Marker profiles of human leukemia and lymphoma cell lines. J Cancer Res Clin Oncol 101:91–100.

Mommsen S, Aagaard J, Sell A (1983): An epidemiological study of bladder cancer in a predominantly rural district. Scand J Urol Nephrol 17:307–312.

Morgan RW, Wong O (1984): An epidemiologic analysis of the mortality experience of Mobil Oil Corporation employees at the Beaumont, Texas, refinery. Report submitted to Mobil Oil Corporation.

Morgan RW, Wong O (1985): Final report. An epidemiological mortality study of Mobil Oil Corporation employees at the Paulsboro, New Jersey, refinery. Report submitted to Mobil Oil Corporation.

Morgan RW, Wong O (1985): A review of epidemiological studies on artifical sweeteners and bladder cancer. Food Chem Toxicol 23:529–533.

Morgan RW, Foliart DE, Wong O (1985): Asbestos and gastrointestinal cancer: A review of the literature. West J Med 143:60–65.

Nakamura K (1987): An epidemiological study of refinery workers. Department of Industrial Epidemiology, National Institute of Industrial Health, Kawasaki, Japan.

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Nelson NA (1985): Mortality in Amoco,Oil refinery employees. Phase I. TSCA Section 8 (e) Report 8EHQ-0585-0557.

Nelson N, Levin RJ, Albert RE, Blair AE, Griesemer RA, Landrigan PJ, Stayner LT, Swenberg JA (1986): Contribution of formaldehyde to respiratory cancer. Environ Health Perspect 70:23–35.

Raabe GK (1983): Kidney cancer epidemiology in petroleum related studies. In Mehlman MA (ed): "Renal Effects of Petroleum Hydrocarbons: Advances in Modern Environmental Toxicology." Vol. VII. Princeton NJ: Princeton Scientific Publishers, Inc., pp 259–271.

Reeve GR, Thomas TL, Kelly VF, Waxweiler RJ, Itaya S (1982): A proportionate mortality study of an oil, chemical, and atomic workers local in Texas City, Texas. Ann NY Acad Sci 381:54–61.

Rushton L, Alderson MR (1981a): An epidemiological survey of eight oil refineries in Britain. Br J Ind Med 38:225–234.

Rushton L, Alderson MR (1981b): A case-control study to investigate the association between exposure to benzene and deaths from leukaemia in oil refinery workers. Br J Cancer 43:77–84.

Rushton L, Alderson MR (1983): Epidemiological survey of oil distribution centres in Britain. Br J Ind Med 40:330–339.

Savitz DA, Moure R (1984): Cancer risk among oil refinery workers: A review of epidemiologic studies. J Occup Med 26:662–670.

Schottenfeld D, Worshauer ME, Zauber AG, Meikle JG, Hart BR (1981): A prospective study of morbidity and mortality in petroleum industry employees in the United States—a preliminary report. In Peto R, Schneiderman M (eds): "Banbury Report 9: Quantification of Occupational Cancer." Cold Spring Harbor, NY: Cold Spring Harbor Laboratory, pp 247–265.

Stemhagen A, Slade J, Altman R, Bill J (1983): Occupational risk factors and liver cancer: A retrospective case-control study of primary liver cancer in New Jersey. Am J Epidemiol 117:443–454.

Tabershaw/Cooper Associates, Inc. (1974): A mortality study of petroleum refinery workers project OH-1. Report submitted to the American Petroleum Institute, Washington, DC.

Thériault G, Goulet L (1979): A mortality study of oil refinery workers. J Occup Med 21:367–370.

Thériault G, Provencher S (1987): Mortality study of oil refinery workers: Five-year follow-up. J Occup Med 29:357–360.

Thomas TL, DeCouflé P, Moure-Eraso R (1980): Mortality among workers employed in petroleum refining and petrochemical plants. J Occup Med 22:97–103.

Thomas TL, Waxweiler RJ, Moure-Eraso R, Itaya S, Fraumeni JF, Jr (1982a): Mortality patterns among workers in three Texas oil refineries. J Occup Med 24:135–141.

Thomas TL, Waxweiler RJ, Crandall MS, White DW, Moure-Eraso R, Itaya S, Fraumemi J (1982b): Brain cancer among OCAW members in three Texas oil refineries. Ann NY Acad Sci 381:120–129.

Thomas TL, Waxweiler RJ, Crandall MS, White DW, Moure-Eraso R, Fraumeni JF, Jr (1984): Cancer mortality patterns by work category in three Texas Refineries. Am J Ind Med 6:3–16.

Thorpe JJ (1974): Epidemiologic survey of leukemia in persons potentially exposed to benzene. J Occup Med 16:375–382.

Tsai SP, Wen CP, Weiss NS, Wong O, McClellan WA, Gibson RL (1983): Retrospective mortality and medical surveillance studies of workers in benzene areas of refineries. J Occup Med 25:685–692.

Van Peenen PFD, Blanchard AG, Wolkonsky PM (1984): Smoking habits of oil refinery employees. AJPH 74:1408, 1409.

Wald NJ, Doll R (1985): Interpretation of negative epidemiologic evidence for carcinogenicity. International Agency for Research on Cancer Scientific Publication No. 65. Lyon

Wen CP, Tsai SP, Gibson RL (1982): A report on brain tumors from a retrospective cohort study of refinery workers. Ann NY Acad Sci 381:130–138.

Wen CP, Tsai SP, McClellan WA, Gibson RL (1983): Long-term mortality study of oil refinery workers. I. Mortality of hourly and salaried workers. Am J Epidemiol 118:526–542.

Wen CP, Tsai SP, Gibson RL, McClellan WA (1984a): Long-term mortality of oil refinery workers. II. Comparison of the experience of active, terminated and retired workers. J Occup Med 26:118–127.

Wen CP, Tsai SP, Moffitt KB, Bondy M, Gibson RL (1984b): Epidemiologic studies of the role of gasoline (hydrocarbon) exposure in kidney cancer risk. In Mehlman MA (ed): "Renal Effects of Petroleum Hydrocarbons: Advances in Modern Environmental Toxicology." Vol. VII. Princeton, NJ: Princeton Scientific Publishers, Inc., pp 245–257.

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06692

Wen CP, Tsai SP, Moffitt K, Bondy M, Runion H, Gibson RL (1984c): Leukemia among oil refinery workers and residents in the surrounding communities. (With additional updated tables for leukemia.) Presented at the "Seminar on Cancer Prevention and Control in Texas" in San Antonio, Texas, February, 1984 (sponsored by the Texas Dept. of Health).

Wen CP, Tsai SP, Weiss NS, Gibson RL, Wong O, McClellan WA (1985): Long-term mortality study of oil refinery workers. IV. Exposure to the lubricating-dev ng process. JNCI 74:11–18.

Wong O (1980): An investigation of malignant neoplasms of the brain and other parts of the nervous system among a cohort of petroleum refinery workers. Report submitted to American Petroleum Institute.

Wong O (1987): An industry wide mortality study of chemical workers occupationally exposed to benzene. I General Results. Br J Ind Med 44:365–381.

Wong O, Tabershaw IR (1980): Comments on mortality among workers employed in petroleum refining and petrochemical plants. J Occup Med 22:638–640.

Wong O, DeCouflé P (1982): Methodological issues involving the standardized mortality ratio and proportionate mortality ratio in occupational studies. J Occup Med 24:299–304.

Wong O, Morgan RW, Kheifets L, Larson Sr (1985): Comparison of SMR, PMR and PCMR in a cohort of union members potentially exposed to diesel exhaust emissions. Br J Ind Med 42:435–448.

Wong O, Morgan RW, Bailey WJ, Swencicki RE, Claxton K, Kheifets L (1986): An epidemiological study of petroleum refinery employees. Br J Ind Med 43:6–17.

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