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Industries and cancer

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Epidemiologic evidence on the relationship between selected industries and cancer is reviewed. This article will focus on several industries which have not been covered elsewhere in this volume, briefly describe current research on cancer in the agricultural and construction industries, and discuss surveillance data on cancer mortality in relation to industry listed on US death certificates. Employment in the rubber industry has been associated with bladder cancer, leukemia, stomach, and lung cancer and is considered by the International Agency for Research on Cancer (IARC) to have 'sufficient evidence of carcinogenicity in humans.' Studies of workers exposed to polychlorinated biphenyls (PCBs) have reported excess mortality from gastrointestinal neoplasms, hematologic neoplasms, and skin cancer (specifically malignant melanoma); IARC considers that the evidence for carcinogenicity in humans is 'limited.' Employment in the boot and shoe industry has been associated with nasal adenocarcinomas in England and Italy ('sufficient'). Hairdressers and barbers have been found to have excess bladder cancer and less consistent evidence for several other sites ('limited'). Workers exposed to wood dust have excess mortality from cancer of the nasal sinuses and paranasal cavities; there is less consistent evidence for excess laryngeal cancer'('sufficient'). Workers employed in the petroleum industry have limited evidence for excess leukemia and other lymphatic and hematopoietic neoplasms, and skin cancer (particularly malignant melanoma) ('limited'). *Cancer Causes and Control* 1997, 8, 356-370

Key words: Cancer, industries.

Introduction

The literature concerning industries and cancer is vast, encompassing retrospective cohort and proportionate mortality studies aimed at characterizing the mortality experience of particular industries, industry-specific studies directed at understanding the health effects of exposure to a particular substance (*e.g.*, garment workers exposed to formaldehyde), population-based case-control studies examining the relationship between occupation and risks of specific cancers, and surveillance studies. This article will not attempt a comprehensive review of associations that have been reported between industries and site-specific cancers, but instead will focus on several major topics that have not been covered elsewhere in this volume (the rubber industry; polychlorinated biphenyls (PCBs) in the electrical industry; boot and shoe manufacture and repair; hairdressers and barbers; wood dust; and the petroleum industry). In addition, we will briefly discuss cancer risks in other industries.

For each of the major topics, the review will focus on studies published after the most recent comprehensive review in the International Agency for Research on Cancer (IARC) *Monograph* series. For most topics, the methodology and results of retrospective cohort mortality studies will be summarized in tables and relevant findings from other types of studies will be discussed in the text. Tables will include study findings that are statistically

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significant ($P < 0.05$, lower bound of 95 percent confidence interval [CI] > 1.00); other relevant findings will be discussed in the text. A systematic attempt was made to identify all published cohort mortality and PMR studies of industrial cohorts relevant to each topic. When multiple updates of a cohort study have been published, only the most recent was included in the review.

Rubber workers

In 1982, IARC evaluated the strength of available evidence regarding cancer excesses in the rubber industry.[1] IARC concluded that the evidence was *sufficient* for excess occurrence of bladder cancer and leukemia in rubber workers and *sufficient* for causal association with occupational exposures, *sufficient* for excess occurrence of stomach and lung cancer, and *limited* for causal association with occupational exposures, and limited or inadequate with respect to other cancer sites.[1]

Retrospective-cohort mortality studies published in 1981 or later are summarized in Table 1.[2-13] Of particular note is a series of studies by Delzell and Monson[10-14] which analyze mortality within different departments of a large rubber-manufacturing company located in Akron, Ohio, United States. These studies confirmed earlier associations of leukemia, and lung and stomach cancer with employment as a rubber worker, and identified site-specific cancer excesses in different process areas. For example, stomach cancer was elevated among front-processing workers who are exposed to particulates generated during mixing of dry ingredients, and to fumes and reaction products emitted during milling; leukemia was elevated only in back-processing workers who are exposed to solvents used in extrusion and calendering.[11] Excesses in lymphoma and multiple myeloma were found in industrial products workers and reclaim (processing of scrap rubber) workers in the Akron cohort.[11,13] Mortality from bladder cancer was not elevated significantly in most of the cohorts and subcohorts studied, which may reflect a reduction in risk due to phasing out of recognized aromatic amine carcinogens such as 2-napthylamine by the 1950s. Although some mortality studies did not report any significant associations, the sites found to be in excess in recent studies are generally consistent with earlier ones (Table 1).

Case-control studies also have been conducted within rubber worker cohorts. Delzell *et al*[14] conducted a case-control study of lung cancer in a rubber-products manufacturing plant (not the plant described above). This study found that employment in Reclaim Operations and Special Products (manufacture of fuel cell, rocket liner, and aerospace products) was associated with an increased risk of lung cancer. Bourguet *et al*[15] conducted a case-control study of squamous cell carcinomas of the skin among employees of two rubber companies located in Akron. Exposure to rubber stock and lubricating oils was associated with increased skin cancer risk. Two small studies were conducted to examine the association of lymphocytic leukemia risk with solvent exposures in the rubber industry. Arp *et al*[16] studied 15 lymphocytic leukemia cases and 30 controls and found an association with jobs entailing direct handling of benzene and other coal-derived organic solvents. Checkoway *et al*[17] analyzed 11 lymphocytic leukemia cases and 1,350 controls and examined 24 specific solvents. This study found significant associations with exposure to carbon disulfide, carbon tetrachloride, acetone, hexane, and methanol.

In recent years, hazards associated with the manufacture of styrene-butadiene rubber have received increasing attention. Styrene-butadiene rubber represents 40 percent of all rubber produced in the US.[18] IARC has concluded that there is *limited* evidence of the carcinogenicity of butadiene in humans and *sufficient* evidence of the carcinogenicity of butadiene in experimental animals;[19] while styrene was found to have *inadequate* evidence for carcinogenicity in humans and *limited* evidence in animals.[19] Recently, a study by Delzell *et al*[21] of 15,649 workers employed 1943-91 at eight styrene-butadiene plants in the US and Canada found a significant excess of leukemia which was associated with estimated cumulative exposure to butadiene.[20]

Polychlorinated biphenyls (PCBs)

The carcinogenicity of PCBs was reviewed by IARC in 1978,[22] and updated in 1987.[23] In 1987, IARC viewed the evidence for carcinogenicity to humans as *limited*, and to animals as *sufficient* and classified PCBs in Group 2A, as probably carcinogenic to humans.

Relatively few occupational cohorts have been studied for mortality or cancer incidence (Table 2). Gustavsson[24] examined mortality among 142 Swedish capacitor workers who were exposed to PCBs and found no excess of cancer deaths, site-specific cancer deaths, or cancer incidence. In 1987, Bertazzi *et al*[25] examined workers in the production department at a northern Italian electrical-capacitor manufacturing plant who worked there a minimum of six months. This study found significant excesses of deaths from malignant neoplasms of the gastrointestinal tract in male workers and hematologic neoplasms in both male and female workers. Brown *et al*[26] conducted a mortality study of highly exposed workers (about 10 percent of the total workforce) in plants in New York state and Massachusetts (US) which produced electrical capacitors. An excess in mortality from cancer of the liver, gall bladder and biliary tract was observed which was restricted largely to female workers in the Massachusetts plant. *Sinks et al*[27]

Table 1. Retrospective cohort studies of workers in the rubber industry published in 1981 or later

Author (ref) Year	Population and selection criteria	No. of subjects	Total no. of deaths	Cohort or subcohort	Occurrence of cancer		SMR[a]	(CI)[b]
					Site	No.		
Norseth *et al*[2] 1983	Footwear and tire plant in Norway, employed at least 18 m, followed 1953-78	2,448	Unknown	Workshop/ maintenance	Pancreas	6	6.7	(2.5-14.5)
Gustavsson *et al*[3] 1984	Two tire and industrial rubber goods plants in Sweden, 1983 employed at least 12 m, followed 1952-81	12,212	9,112	≥ 20 years	Lung	9	2.4	(1.1-4.5)
Wang *et al*[4] 1984	Two rubber tire factories in Shanghai, selection and follow-up period unclear	Unknown	Unknown	Mixing & milling	Lung	[illegible]	2.7	(1.0-5.9)
				Mixing & milling	Lung	[illegible]	5.6	(1.2-16.2)
Bernardinelli *et al*[5] 1987	Tire manufacturing company in north Italy, worked at least 1 yr, followed 1962-79	5,068	143	Total	Liver	2	5.2	(0.6-18.7)
					Peritoneum	2	5.4	(0.6-19.3)
					Max. sinus	1	37.3	(0.9-207)
					Prostate	2	5.2	(0.6-18.7)
Sorahan *et al*[6] 1989	Thirteen large rubber factories in Great Britain, employed 1946-60; followed 1946-85	36,691	11,765	Total	Pharynx	30	1.5	(1.0-2.1)
					Esophagus	107	1.2	(1.0-1.5)
					Stomach	359	1.1	(1.0-1.2)
					Lung	1,592	1.3	(1.2-1.4)
Delzell *et al*[7] 1981	Automobile tire plant in Connecticut (US), 1981 employed at least 2 yrs, followed 1954-77	1,792	249	—	No significant excesses			
Holmes *et al*[8] 1986	Butyl manufacturing plant in Louisiana (US), employed at least 1 m, followed 1943-78	852	179	—	No significant excesses			
Carlo *et al*[9] 1993	Passenger tire manufacturing facility in Texas (US), employed at least 1 yr, followed 1962-89	2,30[illegible]	102	—	No significant excesses			
Delzell & Monson[10] 1982	Processing workers in a rubber tire manufacturing company in Akron, OH (US) worked at least 2 yrs, followed 1940-78	2,666	1,131	All processing	Biliary/liver	12	2.0	(1.[illegible]-3.6)
					Leukemia	16	1.7	(1.[illegible]-2.8)
Delzell & Monson[11] 1984	Industrial products workers in a manufacturing company in Akron, OH (US), worked at least 2 yrs, followed 1940-78	6,533	9,110	All industry processing	Other lymphatic & multiple myeloma	18	1.7	(1.[illegible]-2.7)
Delzell & Monson[12] 1985	Curing workers in a manufacturing company in Akron, worked at least 2 yrs, followed 1940-78	1,150	547	All curing	Lung	45	1.5	(1.1-2.0)
Delzell & Monson[13] 1985	Reclaim workers in a manufacturing company in Akron, OH (USA), worked at least 2 yrs, followed 1940-78	1,790	539	All reclaim	Esophagus	6	2.7	(1.0-5.8)
					Other lymphatic & multiple myeloma	7	3.6	(1.4-7.4)

[a] SMR = standardized mortality ratio.

[b] CI = 95% confidence interval.

Table 2. Retrospective cohort studies of workers exposed to polychlorinated biphenyls (PCB) published in 1982 or later

Author (ref) Year	Population and selection criteria	No. of subjects	Total no. of deaths	Cohort or subcohort	Occurrence of cancer		SMR[a]	(CI)[b]
					Site	No.		
Gustavsson *et al*[24] 1986	Capacitor production workers in Sweden employed at least 6 m, followed 1960-79	142	21	—	No significant excesses			
Bertazzi *et al*[25] 1987	Capacitor production workers in northern Italy, employed 1946-78 for at least 1 w; followed 1946-83	2,100	64	Males *cf* local referents	Malignant tumors	14	1.8	(1.0-3.0)
					GI tract	6	2.7	(1.1-5.7)
					Hematologic neoplasms	3	2.6	(0.5-7.7)
				Females	Malignant tumors	12	2.3	(1.2-3.8)
					Hematologic neoplasms	4	3.8	(1.1-8.8)
Brown *et al*[26] 1987	Capacitor production workers in NY state and Massachusetts (US), employed at least 3 m in PCB-exposed job; followed 1940-82	2,588	295	Total	Liver, gallbladder, biliary tract	5	2.6	(0.8-6.1)
Sinks *et al*[27] 1992	Capacitor manufacturing workers in Indiana (US), worked at least 1 day; followed 1957-86	3,643	192	Total	Skin	8	4.1	(1.8-8.0)
Yassi *et al*[28] 1994	Transformer manufacturing workers in Canada, male workers employed for at least 1 m; followed 1946-75	2,222	138	Definite death match	Pancreas	7	2.9	(1.2-6.0)
				All death match	Pancreas	11	5.0	(2.5-8.9)

[a] SMR = standardized mortality ratio.

[b] CI = 95% confidence interval.

Table 3. Proportionate mortality and retrospective cohort studies of workers employed in shoe or boot manufacturing, published after 1981

Author (ref) Year	Population & selection criteria	No. of subjects	Total no. of deaths	Cohort or subcohort	Occurrence of cancer		PMR[a] or SMR[b]	(CI)[c]
					Site	No.		
Decouflé & Walrath[38] 1983	Deaths among workers in US shoe manufacturing plants represented by 2 unions, 1966-77	NA	3,754	Males	Esophagus	16	1.7	(1.0-2.7)
					Rectum	22	1.6	(1.0-2.4)
					Liver, gallbladder	14	1.8	(1.0-3.0)
					T,B, & L[d]	155	1.2	(1.0-1.4)
				Females	Rectum	19	1.8	(1.1-2.8)
					Liver, gallbladder	17	2.0	(1.0-3.2)
					Pancreas	28	1.5	(1.0-2.2)
					Cervix	32	1.9	(1.0-2.7)
Gambrant & Wegman[9] 1984	Decedents who had resided in 3 towns in Massachusetts (US), died 1954-74 and had 'shoe manufacturing' as occupation on death certificate	NA	1,962	Males	Digestive	84	1.4	(1.1-1.7)
				Females	Bladder	7	2.5	(1.2-5.1)
Walrath *et al*[4] 1987	Deaths 1960-89 among employees of a shoe manufacturing company, identified through obituaries	NA	4,734	Males	Stomach	71	1.8	(1.4-2.3)
					Colon	100	1.5	(1.2-1.9)
					Rectum	33	1.4	(1.0-2.0)
					Bone	6	2.2	(0.8-4.8)
					Multiple myeloma	10	1.9	(0.9-3.5)
				Females	Colon	49	1.4	(1.0-1.9)
					Rectum	16	2.0	(1.1-3.2)
					Multiple myeloma	8	3.5	(1.5-6.8)
Pipard & Acheson[43] 1985	Workers employed in boot and shoe manufacturing in 3 towns in Great Britain, followed through 1982	5,017	3,434	Total	Nasal cancer	10	5.4	(2.6-9.8)
					Leukemia	5	2.4	(0.9-4.9)
Paci *et al*[44] 1986	Workers employed 1950-84 at a shoe manufacturing plant in Florence, Italy	2,013	222	Males	Stomach	17	2.4	(1.4-3.8)
					Leukemia	6	4.0	(1.5-8.7)
				Females	No significant excesses			
Walker *et al*[45] 1993	Workers employed at least 1 m 1940-79, followed through 1982	7,814	1,545	Males	T,B, & L[d]	68	1.6	(1.2-2.0)
				Females	No significant excesses			

[a] PMR = proportionate mortality ratios.
[b] SMR = standardized mortality ratios.
[c] CI = 95% confidence interval.
[d] T,B, & L = trachea, bronchus, and lung.

studied a cohort of workers potentially exposed to Aroclor **1242** and Aroclor 1016 in the manufacture of capacitors. **A** significant excess of deaths from skin cancer was found which was entirely due to deaths from malignant melanoma. **A** nonsignificant excess of brain cancer deaths ($n = 5$, standardized mortality ratio [SMR] = 1.8) also was noted. The risk of melanoma did not vary by duration of employment, time since first employment, or estimated cumulative PCB exposure. The risk of brain cancer increased with duration of employment and cumulative PCB exposure. Yassi et *al*[28] reported on the mortality of transformer manufacturing workers who were exposed to 'Askerols' (transformer fluid containing PCBs) and mineral oils. The study found an elevated risk of mortality from pancreatic cancer which was concentrated among workers employed more than six months (SMR = *7.6)* and those who were involved in transformer assembly (SMR = 12.9). A preliminary report[29] noted an increase in deaths due to malignant melanoma (two observed *cf* 0.04 expected) and cancer of the pancreas among 51 research and development employees and 41 refinery plant employees with potential exposure to Aroclor 1254 and other potentially toxic and carcinogenic compounds at a New Jersey (US) petrochemical facility. A cluster of adenocarcinoma of the kidney was reported based on the diagnosis of **this** rare cancer in three male utility workers who were responsible for maintaining electrical transmission equipment including power transformers.[30] Potential exposures among these workers included organic solvents, herbicides, electromagnetic fields, and PCBs.

Recent data have suggested that some PCBs have estrogenic effects, and raised concern that PCB exposure may increase risk of breast and endometrial cancer, although mortality studies of occupationally exposed cohorts, to date, have not demonstrated an increased risk." Data suggesting an association between PCB exposure and breast cancer were obtained from case-control studies[32,33] in the general population in which levels of PCB and other organochlorine compounds were measured in mammary adipose tissue or stored sera; a more recent study" did not find elevated PCB levels in sera of cases compared with controls. The association between PCB exposure and breast cancer currently is being investigated in the capacitor manufacturing plants previously studied by Brown[76] and Sinks *et al*;[27] the Brown cohorts have been expanded to include all workers employed for three months, yielding **13,736** women, and breast cancer incidence as well as mortality will be studied.[35,36]

Boot and shoe manufacture and repair

IARC reviewed boot and shoe manufacture and repair in 1981[37] and updated its review in 1987.[23] In 1981, IARC concluded that there was sufficient evidence for the carcinogenicity of employment in the boot and shoe industry. Based on the epidemiologic literature at the time, IARC concluded that employment in this industry was 'causally related' to the development of nasal adenocarcinomas, for which elevated risks had been reported in England and in Italy. IARC also noted that there was evidence of an increased risk of bladder cancer associated with employment in the leather industry, but it was not possible to separate workers in the 'boot and shoe' industry from other leather workers. It also was noted that the occurrence of leukemia and aplastic anemia among shoemakers exposed to benzene had been well-documented.

Since the 1981 IARC review, three large studies using proportionate mortality ratios (PMR) in US populations have shown no excess of nasal cancer. Decoufle and Walrath[38] studied members of two US labor unions who had worked in shoe manufacturing. No deaths from nasal cancer were found, whereas 2.2 were expected. No excess mortality was observed from leukemia or bladder cancer. However, deaths from malignant neoplasms of several digestive organs and lung cancer were elevated among men, and deaths from malignant neoplasms of several digestive organs and cancer of the cervix uteri were elevated among women.

Garabrant and Wegmen[39] studied death certificates from three towns in Massachusetts in which the shoe and leather industries were major employers. Deaths among workers in the 'leather industry' were analyzed separately from deaths among workers in the 'boot and shoe' manufacturing industry, thus only the latter are reported here. Men were reported to have elevated numbers of deaths from 'all digestive' cancers, while women had elevated numbers of deaths from bladder cancer. There were no deaths from cancer of the nose or paranasal sinuses, and the number of deaths from leukemia was less than the number expected, for both men and women.

Walrath et *al*[40] studied former employees of a large shoe manufacturing company in upstate New York and found significantly elevated PMR for malignant neoplasms of the stomach, colon, rectum, bone, and multiple myeloma among men, and colon, rectum, and multiple myeloma among women. There were no deaths from nasal cancer as an underlying cause of death (1.9 expected); one nasal cancer was recorded as a non-underlying cause of death, and two deaths from nasopharyngeal cancer were included in cancers of the 'buccal cavity and pharynx.' There was no excess risk of bladder cancer or leukemia. Surveillance of nasal cancer incidence in the Northamptonshire area of England demonstrated an increasing incidence during the period 1950-79; workers entering the industry as recently as 1932-40 continued to have a relatively high risk of nasal cancer.[41] Decouflé and Wal-

rath[42] reviewed methodologic reasons for the differential risk of nasal cancer between workers in the British and US shoe industries, and concluded that the underlying risk in US workers, if present, is likely to be smaller in magnitude than that seen in the British industry.

There have been three cohort studies published since the 1981 IARC review. Pippard and Acheson" studied boot and shoe workers residing in three towns in Great Britain. An elevated risk of nasal cancer was found in the cohort overall, which was most pronounced in workers employed in the finishing department (*n* = 5, SMR = 14.1, CI = 4.6-32.9) where exposure to leather dust occurs. An elevated risk of leukemia in the total cohort was concentrated among workers in the 'lasting and making' department (*n* = 3, SMR = 5.7, CI = 1.2-16.5). Workers in the lasting and making departments handled glues, and had potential exposure to solvents including benzene, carbon tetrachloride, trichloroethylene, and carbon disulfide. One of the three plants studied had a significant excess of rectal cancer among workers in the 'lasting and making' department. Paci *et al*[44] conducted a study in a shoe manufacturing plant in Florence, Italy where benzene-containing glues had been used from 1953-60. Excess stomach cancer and leukemia were observed among male workers, while no significant excesses were observed among women. An excess risk of aplastic anemia (*n* = 6, SMR = 15.7, CI = 5.5-32.6) also was observed among male workers. Walker *et al*[45] studied mortality at a US shoe factory in which benzene was never used, and may have been present only as a contaminant of toluene. The only significant excess was for cancer of the trachea, bronchus, and lung among men.

Hairdressers and barbers

IARC reviewed the carcinogenicity of employment as a 'hairdresser or barber' in 1993 and concluded that there is limited evidence that this occupation entails exposures that are carcinogenic.[46] The most consistent evidence was found for bladder cancer with significant excesses in three of six large cohort studies. Other sites for which there was some evidence of an excess included lung cancer, non-Hodgkin's lymphoma, ovarian cancer, and cancers of the buccal cavity and pharynx.

Skov and Lynge[47] reported cancer incidence (1970-87) among 1,177 men and 4,160 women who gave their occupation as hairdresser in the 1970 census in Denmark. Bladder cancer incidence was elevated significantly among men (*n* = not given, relative risk [RR] = 1.6, CI = 1.2-2.0). The risk of non-Hodgkin's lymphoma was increased significantly among women (RR = 1.9, CI = 1.1-3.1). One additional study, published in 1994, combined data from four cancer incidence studies conducted among female hairdressers in Scandinavian countries (Sweden, Norway, Finland and Denmark).[48] An excess of ovarian cancers was found in the combined cohort (*n* = 127, SIR = 1.2, CI = 1.0-1.4) but only Denmark (SIR = 1.2, *n* = 36) and Finland (SIR = 1.9, *n* = 33) contributed to this excess.

A large case-control study of multiple myeloma (689 case patients and 1,681 controls) in four Surveillance, Epidemiology and End Results (SEER) registry areas in the US found no significant associations with employment as a hairdresser or barber." A review article, published in 1995, found a relative risk (RR) of 1.4 (183 observed and 129 expected) for bladder cancer in a pooled analysis of seven cohort studies, and an RR of 1.2 (100 observed and 84.4 expected) for lymphoid neoplasms in a pooled analysis of nine cohort studies, with an RR of 1.5 for non-Hodgkin's lymphoma (17 observed *cf* 11.2 expected).[50]

Wood dust

IARC reviewed wood dust in 1995[51] and concluded that there is sufficient evidence in humans for the carcinogenicity of wood dust but ***inadequate*** evidence in animals. IARC noted that most of the available cohort and case-control studies found associations between exposure to wood dust and cancer of the nasal cavities and paranasal cavities; the magnitude of some RRs was very high. A clear association between exposure to hardwood dust and adenocarcinoma of the nasal cavities and paranasal sinuses was demonstrated; smaller risks were associated with softwood exposure, but exposure to hardwoods could not be ruled out. Case-control studies of laryngeal cancer consistently have shown an association with exposure to wood dust or woodworking, while cohort studies have not found excess mortality from laryngeal cancers. A pooled analysis of five cohort studies, published after the IARC review, found a significant excess of nasopharyngeal cancer (*n* = 9, SMR = 2.4, CI = 1.1-4.5) and nasal cancer (*n* = 11, SMR = 3.1, CI = 1.6-5.6).[52] Some support for an excess risk of multiple myeloma also was reported. The authors concluded that future studies should develop better indicators of exposure and identify incident cases rather than deaths.

Petroleum industry

In 1989, the IARC reviewed 'occupational exposures in petroleum refining' and concluded that there was *limited* evidence that working in petroleum refineries entails a carcinogenic risk.[53] The limited evidence applied to skin cancer and leukemia; for all other cancer sites on which information was available, the evidence was considered inadequate. Other cancer sites for which epidemiologic data were described included malignant neoplasms of the

Table 4. Cohort mortality studies of petroleum industry workers published in 1987 or later

Author (ref) Year	Population and selection criteria	No. of subjects	Total no. of deaths	Cohort or subcohort	Occurrence of cancer		SMR[a]	(CI)[b]
					Site	No.		
Divine & Barron[60] 1987	Employees who worked at least 6 m at a US producing or pipeline location 1946-80; followed through 1980	11,098	1,886	Producing workers Pipeline workers	Thyroid No significant excesses	4	4.8	(1.2-12.4)
Dagg *et al*[61] 1992	Employees who worked at least 1 yr 1950-80 in two California (US) refineries; followed through 1986	14,149	3,228	Richmond, CA, ≥ 30 yrs	Lymphatic & hematopoietic	27	1.5	(1.0-2.2)
Shallenberger *et al*[62] 1992	Employees who worked at least 1 m 1970-82 at three US refineries; followed through 1992	25,321	5,119	Baton Rouge, LA (USA)	Kidney	18	1.9	(1.1-3.1)
Schattner *et al*[63] 1992	Worked at least 1 yr 1964-83 and annuitants alive 1964 at a Canadian chemical company; followed through 1983	34,597	3,909	Total Upstream operating	Malignant melanoma Malignant melanoma	16 6	1.9 6.0	(1.1-3.0) (2.2-13.2)
Schattner *et al*[64] 1993	Worked at least 1 yr 1964-83 and annuitants alive 1964 at petroleum marketing and distribution centers throughout Canada; followed through 1983	6,672	1,154	Tank truck drivers	Leukemia	5	3.3	(1.1-7.8)
Rushton[65] 1993	Worked at least 1 yr 1950-75 at 8 refineries in the UK; followed through 1989	34,569	10,193	Total Laborers	Malignant melanoma Stomach Lung	30 88 254	1.8 1.5 1.1	(1.2-2.5) (1.2-1.8) (1.2-1.8)
Rushton[66] 1993	Worked at least 1 yr 1950-75 in distribution centers in the UK; followed through 1989	23,306	8,473	—	No significant excesses			
Wong *et al*[67] 1993	Exposed to gasoline at least 1 yr, in land based terminals, shipping centers or marine vessels 1946-85; followed through 1989	18,135	17,487	—	No significant excesses			
Tsai *et al*[68] 1993	Worked at least 6 m 1973-89 and pensioners alive in 1973 at refineries in California (US); followed through 1989	4,585	1,051	—	No significant excesses			
Honda *et al*[69] 1995	Worked at least 6 m 1942-84 at a petroleum manufacturing plant in Illinois (US)	9,796	3,627	Total	Mesothelioma	8	3.2	(1.2-6.3)
Tsai *et al*[70] 1996	Worked at least 3 m 1948-89 at a refinery and chemical plant in Texas (US); followed through 1989	9,720	1,737	Refinery	Lymphatic & hematologic Lymphatic & reticulosarcoma	15 6	2.3 6.7	(1.3-3.7) (2.5-14.7)

[a] SMR = standardized mortality ratio.

[b] CI = 95% confidence interval.

brain, stomach cancer, kidney cancer, cancer of the prostate, lung cancer, and cancer of the bone.

Several other reviews of the epidemiologic literature on petroleum refining and/or meta-analyses were published in the 1980s.[54-57] Evidence for elevated skin cancer was derived from case reports, from three refinery cohorts (one of which reported that the excess was due to malignant melanoma) and from one case-control study of malignant melanoma.[53] Evidence of elevated lymphopoietic and hemotopoietic neoplasms was reported by a number of cohort studies, but the sites were inconsistent.[53] Many observations made in the 1980s by reviewers of the epidemiologic literature on the petroleum industry still apply today. In reviewing the epidemiologic literature in 1984, Savitz and Moure[54] pointed out that "the results were markedly inconsistent across studies." An important methodologic concern was that exposure definition was very weak, "failing even to identify which chemicals are involved."[54]

Eleven studies have been published since the IARC review, excluding two first publications of studies which were subsequently updated.[58,59] Five of the 11 studies were updates of studies first published before 1980. The methodology and results of the studies are summarized in Table 4607070 As in previous studies, site-specific excesses were generally inconsistent. Two studies in different populations reported statistically significant elevated SMRs for malignant melanoma;[63,65] one other reported a nearly significant excess among marketing distribution workers ($n = 6$, SMR = 2.6, CI = 0.96-5.7) (1987). Tsai *et al*[71] reported a fourfold excess of mesothelioma mortality among maintenance employees at a refinery/chemical plant complex.

Interest in the possibility that gasoline causes kidney cancer was stimulated by a bioassay which found that male rats exposed to vaporized unleaded gasoline experienced an excess of renal tumors, with some suggestion of a dose-response." Although further toxicologic research indicated that the excess kidney cancer in the male rat was due to a unique gender- and- species related protein" the finding stimulated epidemiologic studies to examine the association between gasoline exposure and renal cancer.[74]

A case-control study was conducted by Poole *et al*[75] in a cohort of approximately 100,000 male refinery workers from five petroleum companies.[75] A total of 102 kidney cancers were identified and matched to four controls per case. Each job was assigned semiquantitative ratings for intensity and frequency of exposure to three hydrocarbon categories, and rated for presence or absence of seven other agents. No significant associations were found for particular exposures; however, analyses of the longest job held by each subject found increased risks in laborers ($n = 24$; RR = 1.9, CI = 1.0-3.9), workers in receipt, storage, and movements ($n = 9$; RR = 2.5, CI = 0.9-6.6), and unit cleaners ($n = 3$; RR = 2.3, CI = 0.5-9.9).

Among the new studies on refinery workers, only one found a significant excess of kidney cancer which was concentrated among 'blue-collar' (nonprofessional) workers.[62] However, several studies found elevated kidney cancer among petroleum distribution workers. The Poole *et al*[75] case-control study found an elevated RR for workers in 'storage and movements.' Rushton[66] found an elevated SMR for kidney cancer among distribution workers ($n = 53$, SMR = 1.2, CI = 0.9-1.6) and an even higher one for drivers ($n = 25$, SMR = 1.4, CI = 0.9-1.6). Schnatter *et al*[63] reported nonsignificant elevation in distribution workers overall ($n = 9$, SMR = 1.3, CI = 0.6-2.6); the SMR was higher among workers with daily exposure to hydrocarbons ($n = 5$, SMR = 2.1, CI = 0.7-4.8). On the other hand, a large study of land and marine-based distribution centers by Wong *et al*[67] did not find an excess risk of kidney cancer.

Wong *et al*[76] conducted a meta-analysis of cell type-specific leukemia risk among workers in a combined cohort of US and British petroleum workers. Cell type data and distribution by person-years were obtained from the authors of the studies (the number of leukemia cases for which cell type could not be obtained was not reported). No significantly increased risks were found for any of the cell types reported (acute myelogenous leukemia: SMR = 1.0; chronic myelogenous leukemia: SMR = 0.9; acute lymphocytic leukemia: SMR = 1.2; chronic lymphocytic leukemia: SMR = 0.8). As Kriebel *et al*[77] pointed out with reference to a previous meta-analysis, 'the petrochemical industry constitutes not a single hazard, but a large collection of exposures to gasoline hydrocarbons varying by chemical mixture, intensity, and duration. Dilution of true risk estimates, therefore, would result from pooling of findings from studies of qualitatively and quantitatively different exposure experiences.'

Summary, petroleum industry

In summary, the epidemiologic literature on the petroleum industry does not indicate an excess in all cancers or consistent excesses in any specific cancer site. Studies published since the IARC review continue to show limited evidence for leukemia and other lymphatic and hematopoietic neoplasms, and skin cancer (particularly malignant melanoma). Kidney cancer elevations also have been observed, particularly among distribution workers. Cancer risks may differ among refineries and within refineries because exposures differ. In addition to variation by job title and department within refineries, refineries differ from each other with respect to the proportions of different products (gasoline, middle distillates, fuel oil, and others), each of which requires different processes to concentrate or reduce particular chemical

components. The chemical composition of refinery streams also may differ by the source of the crude oil.[78]

Rather than attempting to aggregate information across this diverse industry, a more fruitful approach may be to examine risk factors for cancers found to be in excess in particular refineries.

Agricultural industries

Blair and Zahm[79] reviewed the literature on cancer among persons employed in agriculture. They noted that farmers in many countries experience elevated risks of cancers of the lymphatic and hematopoietic system, skin (melanotic and non-melanotic), soft tissue sarcoma, lip, prostate, and brain cancer. Epidemiologic studies have found specific associations between non-Hodgkin's lymphoma and phenoxy-acid herbicides, leukemia and certain insecticides, ovarian cancer and triazine herbicides, prostate cancer and herbicides, and DDT and cancer of the lung and pancreas.

Etiologic agents other than pesticides which may increase cancer risk in agricultural workers include engine exhaust, fuels and oils, sunlight, mycotoxins, dusts, fertilizers, and zoonotic viruses. Recognizing the need for further study of cancer risks among agricultural workers in the US, government agencies" have initiated a large prospective study of approximately 75,000 pesticide applicators in North Carolina and Iowa. Case-control studies nested within the cohort will allow more detailed exposure assessment than has previously been possible.

Construction industry

Analyses of mortality surveillance data collected from 19 US states have found elevated site-specific risks of cancer associated with skilled construction trades, including bone cancer and melanoma in brick masons; stomach cancer in roofers and brick masons; kidney and bone cancer in concrete/terrazzo finishers; nasal cancer in plumbers; scrotal cancer in electricians; acute myeloid leukemia in boilermakers; rectal cancer in electrical power installers; and lung cancer in structural metal workers." Construction workers potentially are exposed to asbestos, silica, other dusts, solvents and other chemicals; and workers in the skilled trades potentially are exposed not only to the materials used in their own trade but also to 'bystander exposures' present in shared work spaces.[81]

The construction industry presents unique challenges for occupational health research and prevention activities because it involves large numbers of relatively small employers, multi-employer work sites, and a highly mobile workforce. In 1990, the US Congress allocated funds for the National Institute for Occupational Safety and Health (NIOSH) to develop a comprehensive prevention program directed at health problems affecting construction workers. One facet of this program is to conduct union-based PMR studies that will characterize the mortality experience of specific construction trades so that preventive measures can be developed. The first study completed, which involved members of the Laborers' International Union of North America (LIUNA) found elevated PMRs for cancer of the lung, stomach, and thyroid gland.[82] PMR studies are underway for sheet metal workers, ironworkers, carpenters, electrical workers, and bricklayers. In addition, an update of a cohort mortality study of approximately 50,000 members of a US painters union is being conducted.

Other industries

Occupational mortality surveillance studies have been used in setting priorities for occupational cancer research.[83,84] In the US, NIOSH maintains the National Occupational Mortality Surveillance (NOMS) database of death certificate data with coded occupation and industry information.[85] The results of a PMR analysis of the NOMS data are used to identify industries with high proportions of deaths due to selected cancers. Some PMRs are consistent with the findings of earlier studies. Of particular interest are the results for industries for which no other studies have been done.

Most of the NOMS data were collected by the National Center for Health Statistics (NCHS) through a NIOSH, NCHS, and US National Cancer Institute collaborative project that supports the coding by state health departments. Some data were supplied directly to NIOSH by the states. Twenty-eight of the 50 states have participated in the project from 1979 through 1993. Occupation and industry are coded according to the 1980 Bureau of the Census classification system.[86] Cause of death is coded according to the 9th Revision of the International Classification of Diseases.[87] The analysis used in this report included the data from 27 states, 1984-90, for blue-collar workers (Census codes 503-889) aged 18 years and older. Gender-specific, race- and age-adjusted PMRs were calculated for 231 industries. Only Black and White decedents were included because the number of deaths in the other races was small. PMRs were calculated by comparing the proportion of deaths due to a specific cause of death in a specific industry with the proportion of deaths due to that cause in all industries. The CIs were calculated based on the Poisson distribution" if the observed number of deaths was 1,000 or less; otherwise, the Mantel-Haenszel chi-square analysis[89] was used.

The results reported are restricted to cancer causes of death in the US manufacturing industries. Up to five industries with PMRs having a lower CI of at least 100 are reported for selected cancers in Tables 5 (for males)

Table 5. Five highest proportionate mortality ratios (PMR) and 95% confidence intervals (CI) for selected cancer sites within manufacturing industries for men: 27 US states, 1984-90

Peritoneum and pleura				Bladder			
Industry (census code)	No.[a]	PMR	(CI)	Industry (census code)	No.[a]	PMR	(CI)
Ship & boat building & repairing (360)	18	5.4	(3.2-8.6)	Plastics, synthetics, & resins (280)	21	1.7	(1.0-2.6)
Plastics, synthetics, & resins (180)	6	5.4	(2.0-11.7)	Misc. manufacturing industries (391)	38	1.5	(1.0-2.0)
Sugar & confectionery products (112)	3	4.7	(1.0-13.6)	Newspaper publishing & printing (171)	43	1.4	(1.0-1.9)
Miscellaneous nonmetallic mineral & stone products (262)	7	4.2	(1.7-8.6)	Tires and inner tubes (210)	43	1.4	(1.0-1.9)
Petroleum refining (200)	6	3.0	(1.1-6.6)	Beverage industries (120)	47	1.3	(0.9-1.7)

Kidney				Non-Hodgkin's lymphomas			
Industry (census code)	No.[a]	PMR	(CI)	Industry (census code)	No.[a]	PMR	(CI)
Electronic computing equipment (322)	10	3.0	(1.4-5.5)	Office & accounting machines (321)	18	1.7	(1.0-2.7)
Grain mill products (110)	21	1.7	(1.0-2.6)	Engines & turbines (310)	33	1.6	(1.1-2.2)
Radio, TV, & communication equipment (341)	19	1.6	(1.0-2.5)	Grain mill products (110)	25	1.6	(1.0-2.3)
Dairy products (101)	45	1.4	(1.0-1.9)	Tires & inner tubes (210)	47	1.5	(1.1-2.0)
Electrical machinery, equipment & supplies (340-350)	143	1.2	(1.1-1.5)	Primary aluminum industries (272)	40	1.5	(1.1-2.0)

Multiple myeloma & immunoproliferative neoplasms				Myeloid leukemia			
Industry (census code)	No.[a]	PMR	(CI)	Industry (census code)	No.[a]	PMR	(CI)
Electronic computing equipment (322)	6	3.2	(1.2-6.9)	Leather products, except footwear (222)	6	2.8	(1.0-6.0)
Ordnance (292)	13	2.1	(1.1-3.6)	Radio, TV & communication equipment (341)	13	2.1	(1.0-3.6)
Dairy products (101)	37	1.7	(1.2-2.4)	Tires & inner tubes (210)	24	1.8	(1.2-2.7)
Other rubber products & plastics footwear & belting (211)	26	1.7	(1.1-2.5)	Apparel & accessories, except knit (151)	20	1.7	(1.0-2.6)
Iron & steel foundries (271)	42	1.6	(1.1-2.1)	Motor vehicles & motor vehicle equipment (351)	120	1.3	(1.1-1.6)

[a] No. = number of deaths.

and 6 (for females). For those cancers which did not have five industries that met the criteria, the next highest PMR with lower CIs that were 90 or greater were reported. Some sites still had fewer than five industries which met the criteria.

Any time many statistical comparisons are made, a certain number will achieve statistical significance by chance alone; thus, for setting research priorities, it is most useful to examine the results of multiple surveillance systems along with other sources of information on potential exposures in industries or occupations at elevated risk.[84] With this *caveat* in mind, there are a number of findings of interest in the data presented. Significant PMRs for cancer of the liver and intrahepatic bile ducts, bladder cancer, non-Hodgkin's lymphoma, and myeloid leukemia among males in the manufacture of 'tires and inner tubes,' and for cancer of the bladder among women in the 'rubber and miscellaneous plastics products' industry are consistent with the results of some epidemiologic cohort studies of mortality of rubber workers. Excess deaths from malignant neoplasms of the peritoneum and pleura in the 'petroleum refining' indus-

Table 6. Up to five highest proportionate mortality ratios (PMR) and 95% confidence intervals (CI) for selected cancer sites within manufacturing industries for women: 27 US states, 1984-90

Breast				Cervix uteri			
Industry (census code)	**No.[a]**	**PMR**	**(CI)**	**Industry (census code)**	**No.[a]**	**PMR**	**(CI)**
Drugs (181)	45	1.4	(1.0-1.9)	Sawmills, planing mills, & millwork (231)	13	3.4	(1.8-5.9)
Dairy products (101)	30	1.4	(0.9-2.0)	Paperboard containers & boxes (162)	10	2.0	(0.9-3.6)
Newspaper publishing & printing (171)	19	1.4	(0.9-1.9)	Bakery products (111)	20	1.8	(1.1-2.7)
Soaps & cosmetics (182)	37	1.3	(0.9-1.8)	Printing, publishing & allied industries (171-172)	34	1.3	(0.9-1.8)
Scientific & controlling instruments (371)	45	1.3	(0.9-1.7)				

Ovary and other uterine adnexa				Bladder			
Industry (census code)	**No.'**	**PMR**	**(CI)**	**Industry (census code)**	**No.'**	**PMR**	**(CI)**
Soaps & cosmetics (182)	17	2.1	(1.2-3.3)	Plastics, synthetics, & resins (180)	6	2.8	(1.0-6.0)
Miscellaneous fabricated metal products (300)	24	1.4	(0.9-2.1)	Canned & preserved fruits & vegetables (102)	10	2.0	(0.9-3.6)
Electrical machinery, equipment & supplies (342)	110	1.2	(1.0-1.4)	Rubber & miscellaneous plastics products (210-212)	19	1.6	(1.0-2.6)
Apparel & accessories, exc. knit (151)	370	1.1	(1.0-1.3)	Apparel & other finished textile products (151-152)	101	1.1	(0.9-1.4)
Knitting mills (132)	78	1.1	(0.9-1.4)				

Kidney				Brain and nervous system			
Industry (census code)	**No.'**	**PMR**	**(CI)**	**Industry (census code)**	**No.~**	**PMR**	**(CI)**
Electronic computing equipment (322)	6	3.8	(1.4-8.2)	Pulp, paper, & paperboard mills (160)	14	1.9	(1.0-3.2)
Photographic equipment & supplies (261)	5	3.1	(1.0-7.3)	Sugar & confectionery products (112)	11	1.9	(1.0-3.4)
Pottery & related products (230)	9	2.3	(1.1-4.4)	Miscellaneous manufacturing industries (391)	25	1.5	(1.0-2.2)
Miscellaneous food preparations & kindred products (121)	9	2.1	(0.9-3.9)	Motor vehicles & motor vehicle equipment (351)	31	1.4	(0.9-2.0)
Footwear, exc. rubber & plastic (221)	39	1.3	(0.9-1.8)	Yarn, thread & fabric mills (142)	195	1.2	(1.0-1.3)

[a] No. = number of deaths.

try are consistent with some recent studies.[63,69,70]

Other findings are suggestive of cancer risks in industries which have not been extensively investigated. Excesses of kidney cancer and non-Hodgkin's lymphoma among males in the 'grain mill products' industry may be associated with the use of fumigants such as carbon tetrachloride and ethylene dibromide[90,91] which are potential human carcinogens.[92,93] A substantial excess of deaths from kidney cancer was observed in the 'electronic computing equipment' industry for both males (PMR = 3.0, CI = 1.4-5.5) and females (PMR = 3.8, CI = 1.4-8.2); elevated deaths from multiple myeloma also were observed among males in this industry (PMR = 3.1, CI = 1.2-6.9). Exposures in the microelectronics industry include several potentially carcinogenic solvents (carbon tetrachloride, perchloroethylene), potentially carcinogenic metals (arsenic, beryllium, cadmium, chromium, and nickel), asbestos, and reactive chemicals (epichlorohydrin, formaldehyde).[94]

In conclusion, cancer risks are well understood for

some industries, but questions remain about others. Of particular concern are industries (such as the microelectronics industry) which employ new technology or chemicals not in use 25 or more years ago, for which the latency period still is inadequate to detect excess cancer mortality or incidence.

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