[Chan-Yeung and Malo 1993a]. It is not unreasonable to suggest that the natural history of MWF-associated asthma, although not yet well described, is similar to asthma associated with other better studied occupational agents.

In many exposed workers, acute respiratory symptoms and/or modest functional decrements may never develop into clinical asthma. Nevertheless, they are often quite bothersome to the affected workers, even causing him or her to seek medical treatment [Rosenman et al. 1997b]. They can also serve as biomarkers of potentially hazardous occupational exposure that should be better controlled. Furthermore, repeated modest acute airways effects, though apparently reversible upon removal from exposure, may ultimately lead to irreversible impairment and chronic pulmonary disability. No studies have yet been carried out among exposed metalworkers to relate acute decrements caused by MWF aerosols with chronic airways obstruction. In fact, with the exception of one very limited study [Järvholm 1982] and another study now in progress [Kennedy et al. 1995b], there has been no prospective study of long-term change in lung function among metalworkers exposed to MWF aerosols. For a variety of other occupational respiratory hazards, however, gradually emerging evidence has indicated a link between acute and chronic lung function effects [Peters 1974; Wegman et al. 1982; Weill 1984; Tabona et al. 1984; Becklake et al. 1988; Hankinson and Hodous 1983; Christiani et al. 1994; Glindmeyer et al. 1994; Becklake 1995; Schwartz et al. 1996]. It seems entirely plausible that an analogous phenomenon occurs with regard to adverse pulmonary function effects of occupational exposure to MWF aerosol.

5.2 Tumorigenic Effects in Animals

Few animal data have been published on the tumorigenicity of MWFs. NIOSH is aware of only six animal studies that have examined the tumorigenicity of MWFs [Gilman and Vesselinovitch 1955; Desoille et al. 1973; Jepsen et al. 1977; Wang and John 1988; Gupta and Mehrotra 1989; McKee et al. 1990]. Three of these studies reported only findings related to the skin [Gilman and Vesselinovitch 1955; Jepsen et al. 1977; Gupta and Mehrotra 1989]. Of these three studies, one examined unrefined cutting oil [Gilman and Vesselinovitch 1955], one examined solvent-extracted cutting oil [Jepsen et al. 1977], and the third study did not specify how the cutting oil was refined (although the cutting oil was probably highly refined, as the PAH content was only 5.22%) [Gupta and Mehrotra 1989]. The study by Gilman and Vesselinovitch [1955] found that among mice receiving a skin application of soluble cutting oils formulated from unrefined distillates three times weekly for 310 days, 61% developed skin tumors (of whom 22% had carcinomas) compared with no tumors present in the unexposed control group. Jepsen et al. [1977] found that among mice receiving skin applications of solvent-extracted cutting oils, 80% and 0% of mice developed papillomas after exposure to undiluted and diluted soluble oil, respectively. Jepsen et al. [1977] also studied paraffin-based and naphthalene-based straight oil MWFs. They found that 45% and 0% of mice developed

papillomas after exposure to unused and used paraffin-based solvent-refined straight oil MWF (level of refining unspecified), respectively; they also found that 40% and 100% of mice developed papillomas after exposure to unused and used naphthalene-based straight MWF (level of refining unspecified), respectively. Another study found that both unused and used cutting oils were potent skin tumor initiators [Gupta and Mehrotra 1989]. These investigators found that among mice given a single application of the cutting oil and three times weekly application of a promoting agent (12-0-tetradecanoylphorbol 13-acetate [TPA]), 90% and 60% of mice developed benign skin tumors after exposure to unused and used cutting oil.

Three other animal studies examined the tumorigenic effects of MWF exposure on the skin and other organs [Desoille et al. 1973; Wang and John 1988; McKee et al. 1990]. One study of 20 mice receiving a skin application of used cutting oils (type of refining was not specified) one to three times weekly for 6 months found that two developed pulmonary cancer, and one of the two mice also developed skin cancer [Desoille et al. 1973]. None of the 20 control mice developed cancer. In another animal study, pancreatic carcinoma was found in 9 of 40 Wistar rats orally given undiluted "rust-proof cutting fluid" consisting of sodium nitrite, TEA, and polyethylene glycol for 2 years, whereas none of the 40 control rats developed pancreatic cancer ($P<0.01$) [Wang and John 1988]. All three of the components reported to be in the "rust-proof cutting fluid" (sodium nitrite, TEA, and polyethylene glycol) are components that can be found in some MWFs used in the United States. Finally, one other study found no evidence of carcinogenicity from solvent-extracted cutting oils [McKee et al. 1990].

The animal data are limited in the types of MWFs tested and the outcomes examined. The variety and complexity of MWFs are immense. Even within general classes of MWFs, one can find a wide variety in terms of composition and component concentration (see Chapter 2). Understandably, it would be difficult to select "representative samples" of MWFs for use in animal studies whose findings could be generalized to a wide variety of MWFs. To add to the complexity, chronic application of unused MWFs in animal studies would not be representative of worker exposure to in-use fluids.

In conclusion, there is inadequate animal evidence for the carcinogenicity of MWFs currently in use. Because the carcinogenic activity of individual MWFs depends on the severity of processing of the base oils, and because of the nature and concentration of additives and contaminants and the conditions of use, the existing animal data provide only limited usefulness when interpreting the human data.

5.3 Carcinogenic Effects

There has been concern since the 1940s that occupational exposures to some MWFs may be associated with skin and scrotal cancer, and since the 1970s the concern has

included cancer at other organ sites. This chapter provides a review of the epidemiologic studies that examined the association between MWF exposure and cancer.

5.3.1 Criteria for Inclusion

To be included in this review, an article had to be published in a peer-reviewed journal. Articles were identified from computerized database searches, recommendations from reviewers of earlier drafts of the review, and from references cited in relevant articles. Studies providing data on the association between MWF exposure and cancer were grouped into three categories based on their study design: (1) retrospective cohort mortality and cancer incidence studies of MWF-exposed cohorts and associated nested case-control studies, (2) proportionate mortality ratio (PMR) studies of occupational groups exposed to MWF and associated case-control studies, and (3) population-based studies (primarily case-control interview studies of specific cancer sites that examined cancer risks associated with MWF exposure, or with occupations likely to have MWF exposure [metal machinists, grinders, toolmakers]). The category *population-based studies* includes hospital-based case-control studies because their usual intent is to estimate risks in the general population. For fuller discussion about these study designs and their interpretations, the reader is referred to a textbook on occupational epidemiology [Monson 1990] as well as standard epidemiologic textbooks [Mausner and Kramer 1985; Kleinbaum et al. 1982]. To present the results of the review systematically, the data have been summarized by cancer site in both tables and text.

Not included in the reviews by cancer site are hypothesis-generating studies that examined broad occupational categories based on census or death certificate data. The results of such studies have been summarized separately for all sites combined. A single epidemiologic study of genetic endpoints will also be briefly reviewed.

5.3.2 Studies of Cancer in Broad Occupational Groups

Studies have been conducted that evaluated the risks for many specific cancers among many different occupations and/or industries, some of which had the potential for MWF exposure [Hrubec et al. 1992; Guralnick 1963; Howe and Lindsay 1983; Tola et al. 1988; Milham 1983; Petersen and Milham 1980; Gallagher and Threlfall 1983; Williams et al. 1977; Decoufle et al. 1977; Dubrow and Wegman 1984; Bulbulyan et al. 1992; Magnani et al. 1987; Hall and Rosenman 1991; Greenland et al. 1994]. For the most part, the intent of these studies was hypothesis generation. These studies have included populations from many different geographic areas (e.g., United States, United Kingdom, Finland, Canada, Australia, the Netherlands, and Sweden).

Inherent weaknesses of this type of study include the use of broad occupational categories to define MWF exposure, use of potentially inaccurate sources (death certificates, census data) to define the occupation, the large number of associations tested (which

means that some associations are expected to be statistically significant by chance alone and the inability to control for important confounders such as smoking and alcohol. With these limitations in mind, the findings from these studies are important for suggesting the presence of associations between MWF exposure and particular cancers. For each of the following cancer sites, two or more of the studies found significantly increased risks among occupations with potential MWF exposure (e.g. machinists, grinders, and toolmakers), or industries with potential MWF exposure (e.g., machine shops, metal fabrication): esophageal cancer [Magnani et al. 1987; Hall and Rosenman 1991], stomach cancer [Howe and Lindsay 1983; Hrubec et al. 1992], colorectal cancer [Guralnick 1963; Dubrow and Wegman 1984], lung cancer [Milham 1983; Petersen and Milham 1980; Hrubec et al. 1992; Gallagher and Threlfall 1983; Howe and Lindsay 1983], bladder cancer [Milham 1983; Petersen and Milham 1980; Hrubec et al. 1992], leukemia [Petersen and Milham 1980; Howe and Lindsay 1983; Decoufle et al. 1977], and all cancers combined [Hrubec et al. 1992; Gallagher and Threlfall 1983].

5.3.3 Investigations of Selected Cancers

Table 5–5 describes the cohort studies and PMR studies designed to assess the mortality and/or morbidity of MWF-exposed workers (the population based studies are not included in this table since most of them are specific for each cancer site). The Eisen et al. [1992] and Tolbert et al. [1992] studies have the most statistical power to assess the association between MWF exposure and the risk for cancer because the number of subjects with malignant neoplasms in these studies is an order of magnitude larger than in any of the other cohort studies. Tolbert et al. reported the findings for workers employed at Plants I and II, whereas Eisen reported the findings for workers at Plants I, II, and III. To avoid reporting the results for workers from Plants I and II twice, the findings from these plants are summarized from the report by Tolbert et al. [1992] only, and only the findings from Plant III are summarized from the Eisen et al. [1992] report. Tolbert's findings for Plants I and II were used because her analyses examined the cancer risks associated with exposure to specific classes of MWF. For the purpose of tabulating the number of cohort studies reporting site-specific data for each cancer, Plants I and II [Tolbert et al. 1992] are counted as a single "study," and Plant III is counted as a second study [Eisen et al. 1992].

In general, an RR estimate >1.00 is considered to be statistically significant if the lower bound of the 95% CI for the RR estimate was ≥1.00 or if the two-sided *P* value was ≤0.05 (conversely, an RR estimate <1.00 is considered statistically significant if the upper bound of the 95% CI is <1.00, or if the *P* value is ≤0.05). In tabulating the number of studies with significantly positive findings for each site, a study was counted as statistically significant if the RR estimate overall, or in a relevant major subgroup, was statistically significant. Although statistical significance is not the sole criteria of importance in interpreting the results of a single study or summarizing data from multiple studies, it

Table 5-5. Description of the MWF-exposed cohort and proportionate mortality studies

Author	Type of study/ analysis	Study population	Employment criteria for inclusion	Total number of subjects	Number of malignant neoplasms	Years of followup
Acquavella et al. 1993	SMR*	White workers at a metal-working facility in Iowa; 59% held factory jobs (mortality data in following tables includes only the factory workers)	Hired between 1950 and 1967 and employed at least 6 months	White men = 2,664 White women = 966	White = 103	1950–87
Decoufle 1978	SMR	Blue collar workers at a metal machining plant in north central U.S. (machined gray iron castings)	At least 5 yr of employment in oil-mist-exposed jobs between 1938 and 1967	White men = 2,485	139	To 1/1/68
Eisen et al. 1992	SMR	Plant III: Saginaw Steering Gear (manufactures steering gears)	Employed at least 3 yr between 1939 and 1/1/85	White men = 8,983	White = 183	1941–1/1/85
Järvholm and Lavenius 1987	SIR	Grinding and turning department workers employed at a bearing-ring manufacturing plant in Sweden	Exposed at least 5 yr and employed at any time between 1950 and 1966	White men = 792	67	1958–83
Järvholm et al. 1985	SIR	Turning department workers employed at bearing-ring manufacturing plant in Sweden	Employed at any time between 1960 and 1980	White men = 682	24	1960–80

See footnotes at end of table.

(Continued)

Table 5-5 (Continued). Description of the MWF-exposed cohort and proportionate mortality studies

Author	Type of study/ analysis	Study population	Employment criteria for inclusion	Total number of subjects	Number of malignant neoplasms	Years of followup
Mallin et al. 1986	PMR	Workers at a diesel engine and construction equipment manufacturer in Illinois (employed 10+ yr; 461 eligible deaths among union workers)	Died between 1/1/70 and 3/31/82 and employed 10 yr or more; plant began operation in 1946	White men = 351 Black men = 110	White = 92 Black = 36	1970–2/31/82
Park and Mirer 1996	PMR/ MOR	Workers employed at Detroit area engine plants (Plant 1 and Plant 2)	Employed at least 2 yr, active any time between 1966 and 1987, and died between 1/1/70 and 12/31/89	White men = 1,170 Black men = 613	White = 306 Black = 146	1970–12/31/89
Park et al. 1988	PMR/ MOR	Hourly workers at a ball-bearing manufacturing plant in Connecticut (soluble MWFs predominantly used in grinding operations)	Died between 1/1/69 and 7/31/82 and employed 10 yr or more	White men= 616	White = 157	1969–82
Park et al. 1994	PMR/ MOR†	Workers employed in a tool and die area of an automotive stamping and assembly plant	2 yr of employment before 1/1/89	NA	NA	1978–88

See footnotes at end of table.

(Continued)

Table 5-5 (Continued). Description of the MWF-exposed cohort and proportionate mortality studies

Author	Type of study/ analysis	Study population	Employment criteria for inclusion	Total number of subjects	Number of malignant neoplasms	Years of followup
Rotimi et al. 1993	SMR	Hourly workers at Ohio engine manufacturing plants	Employed any time between 1973 and 1986; also, retired and alive as of 1970; no minimum employment	White men = 5,331 Black men = 1,180	White = 178 Black = 60	1970–87
Silverstein et al. 1988	PMR/ MOR	Union workers at a ball-bearing manufacturing plant in Connecticut	Died between 1950 and 1982, and employed 5 yr or more	White men = 1,532	White = 342	1950–6/30/82
Tolbert et al. 1992	SMR	Hourly workers. Plant I:Gear and Axle, Hamtramak (produces axles and gears) Plant II: Hydra-Matic, Ypsilanti (produces transmissions)	Employed at least 3 yr before 1/1/85	White men = 17,743 Black men = 5,641	White = 1648 Black = ~224 (Plant I only)	1941–1/1/85
Vena et al. 1985	PMR	Union workers at an engine plant (machine and assembly) in New York (before 1950, soluble and insoluble MWFs used; increased use of synthetic MWFs in the mid-1950s)	Died between 1/1/70 and 12/31/79 and employed 10 yr or more; plant began operation in 1938	White men = 472 Black men = 37	White = 128	1970–12/31/79

*Abbreviations: NA=not available, MOR=mortality odds ratio, PMR=proportionate mortality ratio, SIR=standardized incidence ratio, SMR=standardized mortality ratio.

†Only the MOR findings from the tool and die area are provided, because the PMR findings were for workers employed in an automotive stamping and assembly plant where MWF exposures were minimal.

is used as a summary measure in this review because it is applicable to all studies and its meaning is widely understood. CIs, which are preferable to *P* values in interpreting epidemiologic data, are provided in this review for studies where they were reported by the authors.

Tables 5–6 through 5–17 summarize the data generated to examine the association between MWF exposure and risk of cancer at specific organ sites. In an effort to keep the tables to a reasonable size, not all of the RR estimates reported by these studies are included. The Tolbert study provides the risk among those ever exposed to each of the specific classes of MWFs, and the remaining studies provide the risk for all workers with potential MWF exposure and (when available) the risk among workers with the highest duration of employment.

This section provides detailed information only for cancer sites for which there is substantial evidence for an association with MWF exposure (skin, larynx, rectum, pancreas, bladder), and two other sites for which there is more limited evidence for such an association (stomach and esophageal). For other sites, statistically significant (positive or negative) findings are briefly summarized. To keep the discussion to a reasonable length, details presented in the tables are not necessarily repeated in the text.

5.3.3.1 Skin and Scrotal Cancer

Case reports

Since the 1940s, evidence has accumulated to support an association between skin (including scrotal) cancer and occupational exposures to MWFs. Several case reports have identified skin cancer among MWF-exposed workers [Henry 1947; Mastromatteo 1955; Cruickshank and Gourevitch 1952; Cruickshank and Squire 1950; Waterhouse 1971, 1972; Kipling and Waldron 1976; Thony et al. 1976; Fife 1962].

Cohort studies

A cohort study of turners employed between 1960 and 1980 at a Swedish company producing bearing rings found that the MWF-exposed turners had an increased risk for squamous cell carcinoma of the skin (observed=5 [four scrotal, and one facial], exposed=0.3, $P<0.001$) [Järvholm et al. 1985] (Table 5–6). Three additional scrotal cancer cases were identified in the 1987 update of this cohort [Järvholm and Lavenius 1987]. The authors suggest that use of soluble oil MWFs is not associated with scrotal cancer because no cases were observed among the grinders who often use soluble oils [Järvholm and Lavenius 1987]. Furthermore, it should be noted that changes in refinery methods since the 1950s have reduced the straight oil content of PAHs, which have been suggested as the causative agent for MWF-associated skin cancer [Järvholm and Easton 1990; McKee et al. 1990]. Because of the high survival rate for nonmelanoma skin cancer, mortality studies are an inappropriate design for studying this cancer. As would be

Table 5-6. Skin/scrotal cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI* or *P*-value	Study population and cancer site
Cohort studies:						
Eisen et al. 1992	Michigan	SMR	10	0.61	0.29, 1.13	White auto workers in Plant I—skin cancer
			11	1.06	0.53, 1.89	White auto workers in Plant II—skin cancer
			7	1.27	0.51, 2.62	White auto workers in Plant III—skin cancer
Järvholm and Lavenius 1987	Sweden	SIR	7	†	†	Turners only—scrotal cancer
Järvholm et al. 1985	Sweden	SIR	5	16.6	$P<0.001$	Turners employed between 1960 and 1980—squamous cell cancer of the skin
Proportionate mortality studies:						
Park et al. 1988	Connecticut	PMR	4	1.88	0.51, 4.80	White—skin cancer
Silverstein et al. 1988	Connecticut	PMR	4	0.92	0.25, 2.34	White—skin cancer
Vena et al. 1985	New York	PMR	1	0.60	NS	Based on U.S. mortality, white—skin cancer

(Continued)

*Abbreviations: CI=confidence interval, NS=not statistically significant, PMR=proportionate mortality ratio, SIR=standardized incidence ratio, SMR=standardized mortality ratio.

†Expected cases of scrotal cancer were too few to make a reliable estimate of risk.

Table 5-6 (Continued). Skin/scrotal cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population and cancer site
Population-based study:						
Rousch et al. 1982	Connecticut	Case control	26	10.5	4.0, 36.9	Workers ever employed as toolmaker, setter, set-up man, hardener, polisher, automatic screw operator, machinist, or machine operator—squamous cell cancer of the scrotum

Table 5-7. Laryngeal cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI* or *P*-value	Study population
Cohort studies:						
Eisen et al. 1992	Michigan	SMR	2	0.77	0.09, 2.79	White auto workers in Plant III
Eisen et al. 1994	Michigan	Nested case control	28	2.23	1.25, 3.98	Highest exposure to straight MWFs
Tolbert et al. 1992	Michigan	SMR	23	1.98	1.26, 2.98	Ever exposed to straight oil, white
			30	1.41	0.95, 2.01	Ever exposed to soluble oil, white
			8	1.57	0.68, 3.09	Ever exposed to synthetic oil, white
			1	0.50	0.01, 2.78	Ever exposed to straight oil, black
			6	0.91	0.70, 1.17	Ever exposed to soluble oil, black
Proportionate mortality studies:						
Mallin et al. 1986	Illinois	PMR	2	1.76	NS	White
Park and Mirer 1996	Detroit area	PMR	1	0.69	0.02, 3.83	Engine Plant 1, white
			4	1.67	0.46, 4.28	Engine Plant 2, white
Vena et al. 1985	New York	PMR	3	1.81	NS	Based on U.S. mortality, white

(Continued)

*Abbreviations: CI=confidence interval, NA=not available, NS=not statistically significant, PMR=proportionate mortality ratio, SMR=standardized mortality ratio.

Table 5-7 (Continued). Laryngeal cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population
Population-based studies:						
Ahrens et al. 1991	Germany	Case control	NA	2.2	0.9, 5.3	Ever exposed to mineral oil
Brown et al. 1988	Texas	Case control	5	0.53	0.18, 1.58	Ever worked as machinists
Haguenoer et al. 1990	France	Case control	7	1.8	NS	Employed in metal work or as mechanic for at least 15 yr
Russi et al. 1997	Connecticut	Case control	81	1.48	1.01, 2.16	High machining fluid exposure versus oral cancer controls
				1.05	0.81, 1.35	High machining fluid exposure versus population controls
Wortley et al. 1992	Washington State	Case control	NA	1.8	0.5, 6.2	Ever employed as grinding, abrading, or buffing operator
			19	1.0	0.5, 1.9	Ever employed in precision metal-working
Zagraniski et al. 1986	Connecticut	Case control	22	2.5	1.2, 5.2	Ever worked as machinist
			17	2.1	1.0, 4.7	Ever worked as metal grinder
Zheng et al. 1992	China	Case control	12	1.2	0.5, 3.1	Usual occupation of blacksmith, machine-tool operator, electrician, or other related worker
			25	0.8	0.4, 1.6	Self-reported exposure to lubricant fumes

Table 5-8. Rectal cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI* or *P*-value	Study population
Cohort studies:						
Decoufle 1978	Michigan	SMR	8	1.25	NS	White
			4	1.29	NS	White, 5+ yr of heavy oil mist exposure
Eisen et al. 1992	Michigan	SMR	7	1.70	0.68, 3.50	White autoworkers in Plant III
Tolbert et al. 1992	Michigan	SMR	37	1.47	1.04, 2.03	Ever exposed to straight oil, white
			51	1.09	0.81, 1.43	Ever exposed to soluble oil, white
			9	0.92	0.42, 1.74	Ever exposed to synthetic oil, white
			1	0.45	0.01, 2.53	Ever exposed to straight oil, black
			3	0.68	0.14, 1.99	Ever exposed to soluble oil, black
Proportionate mortality studies:						
Mallin et al. 1986	Illinois	PMR	2	0.80	NS	White
Park et al. 1988	Connecticut	PMR	11	3.07	1.54, 5.50	White
Silverstein et al. 1988	Connecticut	PMR	14	1.36	0.81, 2.29	White
Vena et al. 1985	New York	PMR	4	1.38	NS	Based on U.S. mortality, white
			4	2.76	$P<0.05$	Employed in engine plant >20 yr

(Continued)

*Abbreviations: NS=not statistically significant, PMR=proportionate mortality ratio, SMR=standardized mortality ratio.

Table 5-8 (Continued). Rectal cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population
Population-based studies:						
Gerhardsson de Verdier et al. 1992	Sweden	Case control	25	2.1	1.1, 4.0	Ever exposed to cutting oils
Siemiatycki et al. 1987	Montreal	Case control	13	0.7	90% CI: 0.4, 1.0	Ever exposed to cutting oils

Table 5-9. Pancreatic cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI* or *P*-value	Study population
Cohort studies:						
Acquavella et al. 1993	Iowa	SMR	11	2.0	0.9, 3.8	Total workforce
			5	3.6	1.2, 8.3	Factory workers employed >10 yr, hired between 1950 and 1959
Decoufle 1978	Michigan	SMR	8	1.05	NS	White
			1	0.27	NS	White, 5+ yr of heavy oil mist exposure
Eisen et al. 1992	Michigan	SMR	8	0.87	0.37, 1.71	White auto workers in Plant III
Rotimi et al. 1993	Ohio	SMR	8	0.91	0.39, 1.79	Engine plant, white
			7	3.03	1.21, 6.24	Engine plant, black
Tolbert et al. 1992	Michigan	SMR	34	0.80	0.55, 1.11	Ever exposed to straight oil, white
			61	0.77	0.59, 1.00	Ever exposed to soluble oil, white
			19	1.03	0.62, 1.61	Ever exposed to synthetic oil, white
			8	1.40	0.60, 2.77	Ever exposed to straight oil, black
			19	1.62	0.98, 2.54	Ever exposed to soluble oil, black
Proportionate mortality studies:						
Mallin et al. 1986	Illinois	PMR	5	1.19	NS	White
			5	3.57	$P<0.05$	Black

(Continued)

*Abbreviations: CI=confidence interval, MOR=mortality odds ratio, NA=not available, NS=not statistically significant, PMR=proportionate mortality ratio, SMR=standardized mortality ratio.

Table 5-9 (Continued). Pancreatic cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population
Proportionate mortality studies (continued):						
Park and Mirer 1996	Detroit area	PMR	10	1.82	0.87, 3.34	Engine Plant 1, white
			11	1.23	0.62, 2.21	Engine Plant 2, white
		MOR	4	3.61	1.04, 12.6	Machining with straight MWF
Park et al. 1988	Connecticut	PMR	8	1.09	0.55, 2.18	White
Silverstein et al. 1988	Connecticut	PMR	24	1.43	0.96, 2.12	White
		MOR	9	3.10	$P = 0.05$	Employed in grinding 10+ yr
		MOR	5	3.71	$P = 0.05$	Employed in machinery 10+ yr
Vena et al. 1985	New York	PMR	11	1.89	$P<0.05$	Based on U.S. mortality, white
			7	2.32	$P<0.05$	Employed in engine plant >20 yr
Population-based study:						
Mack and Paganini 1981	Los Angeles	Incidence	21	1.30	NA	Machinists, white men

Table 5–10. Bladder and lower urinary tract results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI* or *P*-value	Study population and cancer site
Cohort studies:						
Decoufle 1978	Michigan	SMR	6	1.2	NS	White—bladder and lower urinary
			2	0.8	NS	White, 5+ yr of heavy oil mist exposure—bladder and lower urinary tract
Järvholm and Lavenius 1987	Sweden	SIR	7	1.04	0.4, 2.2	Grinders and turners—bladder
Proportionate mortality studies:						
Mallin et al. 1986	Illinois	PMR	2	0.78	NS	White—bladder
Park and Mirer 1996	Detroit area	PMR	6	2.16	0.79, 4.70	Engine Plant 1 workers, white—bladder
			5	1.13	0.37, 2.64	Engine Plant 2 workers, white—bladder
		MOR	7	2.99	1.15, 7.77	Grinding with straight MWF—bladder
		MOR	4	2.86	1.14, 7.18	Machining or heat treat employment—bladder
Park et al. 1988	Connecticut	PMR	1	0.24	0.01, 1.31	White—bladder
Silverstein et al. 1988	Connecticut	PMR	14	1.26	0.75, 2.13	White—bladder

(Continued)

*Abbreviations: CI=confidence interval, MOR=mortality odds ratio, PMR=proportionate mortality ratio, NA=not available, NS=not statistically significant, SIR=standardized incidence ratio, SMR=standardized mortality ratio.

Table 5–10 (Continued). Bladder and lower urinary tract results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population and cancer site
Vena et al. 1985	New York	PMR	7	2.28	$P<0.05$	Based on U.S. mortality, white—bladder
			4	2.76	NS	Employed in engine plant >20 yr—bladder
Population-based studies:						
Claude et al. 1988	Germany	Case control	18	2.25	1.0, 5.6	Ever worked as turner— bladder and lower urinary tract
			43	0.84	0.54, 1.3	Ever employed as metal worker—bladder and lower urinary tract
Coggon et al. 1984	Britain	Case control	52	1.3	0.9, 1.9	Ever had an occupation with potential cutting oil exposure—bladder
			21	1.5	0.8, 2.8	Ever had an occupation with potentially high cutting oil exposure—bladder
Gonzalez et al. 1989	Spain	Case control	31	0.77	0.5, 1.1	Ever worked as toolmaker ≥6 months— bladder
			NA	1.86	1.2, 2.8	Ever worked as machinery adjuster, assembler or mechanic ≥6 months—bladder

(Continued)

Table 5–10 (Continued). Bladder and lower urinary tract results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population and cancer site
Howe et al. 1980	Canada	Case control	NA	2.7	1.1, 7.7	Ever worked as metal machinist—bladder
Malker et al. 1987	Sweden	Case control	322	1.19	$P<0.01$	Toolmakers or machinists in 1960—bladder
Schifflers et al. 1987	Belgium	Case control	34	2.45	1.28, 4.69	All metal workers—bladder
			8	2.57	0.92, 7.16	Turners—bladder
Siemiatycki et al. 1987	Montreal	Case control	47	1.2	90%CI: 1.0, 1.6	Ever exposed to cutting oils—bladder
Population-based studies:						
Silverman et al. 1983	Detroit	Case control	137	1.1	0.8, 1.5	All metal machinists—bladder and lower urinary tract
			32	1.5	0.9, 2.7	Tool and die worker—bladder and lower urinary tract
Silverman et al. 1989a	U.S.	Case control	102	1.3	1.0, 1.7	Ever worked as machinist ≥6 months— bladder
			51	1.4	0.9, 2.1	Ever worked as drill press operator ≥6 months— bladder
Silverman et al. 1989b	U.S.	Case control	26	1.1	0.6, 1.9	Metal machinery workers— bladder

(Continued)

Table 5–10 (Continued). Bladder and lower urinary tract results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population and cancer site
Steenland 1987	Ohio	Case control	11	2.00	NS	Ever worked as grinding machine operator—bladder and lower urinary tract
			45	0.69	$P<0.05$	Ever worked as machinist—bladder and lower urinary tract
Vineis and Magnani 1985	Italy	Case control	16	1.5	0.7, 3.3	Ever employed in machine tools ≥6 months—bladder

Table 5–11. Stomach cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI* or *P*-value	Study population
Cohort studies:						
Acquavella et al. 1993	Iowa	SMR	5	1.4	0.4, 3.2	Total workforce
			2	2.3	0.3, 8.1	Factory workers employed >10 years, hired between 1950 and 1959
Decoufle 1978	Michigan	SMR	17	1.25	NS	White
			11	1.67	NS	White, 5 yr or more of heavy exposure to oil mist
Eisen et al. 1992	Michigan	SMR	4	0.59	0.16, 1.50	White auto workers in Plant III
Järvholm and Lavenius 1987	Sweden	SIR	9	1.11	0.5, 2.1	Grinders and turners
Rotimi et al. 1993	Ohio	SMR	15	2.54	1.42, 4.20	Engine plant workers, white
			2	0.85	0.1, 3.06	Engine plant workers, black
Tolbert et al. 1992	Michigan	SMR	49	1.12	0.83, 1.48	Ever exposed to straight oil, white
			99	1.19	0.97, 1.45	Ever exposed to soluble oil, white
			21	1.28	0.79, 1.96	Ever exposed to synthetic oil, white
			5	0.76	0.24, 1.77	Ever exposed to straight oil, black
			17	1.01	0.59, 1.62	Ever exposed to soluble oil, black

(Continued)

*Abbreviations: CI=confidence interval, MOR=mortality odds ratio, PMR=proportionate mortality ratio, NS=not statistically significant, SIR=standardized incidence ratio, SMR=standardized mortality ratio.

Table 5–11 (Continued). Stomach cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population
Proportionate mortality studies:						
Park et al. 1988	Connecticut	PMR	11	1.99	1.12, 3.54	White
		MOR	8	6.2	*P*=0.05	Nested case-control study—those workers ever exposed to soluble oil
Park and Mirer 1996	Detroit area	PMR	8	2.09	0.90, 4.11	Engine Plant 1 workers, white
			8	1.30	0.56, 2.57	Engine Plant 2 workers, white
		MOR	3	5.13	1.56, 16.9	Cam-/crankshaft department (Plant 1)
Silverstein et al. 1988	Connecticut	PMR	35	1.97	1.43, 2.72	White
			13	3.39	*P*<0.001	Employed in grinding 10 yr or more
Vena et al. 1985	New York	PMR	4	0.91	NS	Based on U.S. mortality, white
			3	1.37	NS	Employed in engine plant > 20 yr
Mallin et al. 1986	Illinois	PMR	6	1.85	NS	White
Population-based studies:						
Chow et al. 1994	Sweden	SIR	376	1.11	NS	Toolmakers and machinists

(Continued)

Table 5–11 (Continued). Stomach cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population
Population-based studies (continued):						
Kneller et al. 1990	China	SIR	191	1.41	$P<0.01$	Metal grinders, polishers, tool sharpeners, machine-tool operators
			193	1.11	NS	Toolmakers, metal pattern makers, metal workers
Siemiatycki et al. 1987	Montreal	Case control	24	1.1	90%CI: 0.8, 1.4	Ever exposed to cutting oils
Other:						
Park 1994	Ohio	MOR	2	9.55	2.3, 40	Ever employed as tool and die worker

Table 5–12. Esophageal cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI* or *P*-value	Study population
Cohort studies:						
Decoufle 1978	Michigan	SMR	4	1.14	NS	White
			1	0.59	NS	White, 5+ yr of heavy oil mist exposure
Eisen et al. 1992	Michigan	SMR	6	1.38	0.50, 3.01	White auto workers in Plant III
Järvholm and Lavenius 1987	Sweden	SIR	2	1.25	0.2, 4.5	Exposed to oil mist at least 5 yr
Tolbert et al. 1992	Michigan	SMR	22	1.18	0.74, 1.79	Ever exposed to straight oil, white
			35	1.03	0.72, 1.43	Ever exposed to soluble oil, white
			8	0.99	0.43, 1.94	Ever exposed to synthetic oil, white
			5	0.76	0.24, 1.77	Ever exposed to straight oil, black
			10	0.72	0.34, 1.32	Ever exposed to soluble oil, black
Proportionate mortality studies:						
Mallin et al. 1986	Illinois	PMR	2	1.01	NS	White
Park et al. 1988	Connecticut	PMR	6	1.85	0.68, 4.02	White
Silverstein et al. 1988	Connecticut	PMR	13	1.83	1.07, 3.12	White
Vena et al. 1985	New York	PMR	3	1.16	NS	Based on U.S. mortality, white
			2	1.43	NS	Employed in engine plant >20 yr

*Abbreviations: CI=confidence interval, PMR=proportionate mortality ratio, NS=not statistically significant, SIR=standardized incidence ratio, SMR=standardized mortality ratio.

Table 5–13. Brain/nervous system cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI* or *P*-value	Study population and cancer site or cell type
Cohort study:						
Decoufle 1978	Michigan	SMR	5	1.5	NS	White—brain and other parts of nervous system
			0	—	—	White, 5+ yr of heavy oil mist exposure—brain and other parts of nervous system
Eisen et al. 1992	Michigan	SMR	7	0.85	0.34, 1.75	White auto workers in Plant III—brain
Tolbert et al. 1992	Michigan	SMR	22	1.08	0.68, 1.64	Ever exposed to straight oil, white— brain
			46	1.24	0.91, 1.66	Ever exposed to soluble oil, white— brain
			6	0.61	0.22, 1.33	Ever exposed to synthetic oil, white— brain
			—	—	—	Ever exposed to straight oil, black— brain
			2	0.77	0.09, 2.78	Ever exposed to soluble oil, black— brain
Proportionate mortality studies:						
Mallin et al. 1986	Illinois	PMR	1	†	—	White—brain, nervous system
Park et al. 1988	Connecticut	PMR	4	1.23	0.34, 3.15	White—brain and other CNS

See footnotes at end of table.

(Continued)

Table 5–13 (Continued). Brain/nervous system cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population and cancer site or cell type
Proportionate mortality studies (continued):						
Silverstein et al. 1988	Connecticut	PMR	6	0.99	0.44, 2.19	White—brain and other CNS
Vena et al. 1985	New York	PMR	2	0.71	NS	Based on U.S. mortality, white—brain and other CNS
Population-based studies:						
Carpenter et al. 1988	U.S.	Case control	28	1.57	NS	Ever exposed to cutting oils while employed at nuclear facilities—CNS cancer
Reif et al. 1989	New Zealand	Case control	NA	0.96	0.13, 7.44	Most recent occupation was as a metal processor (smelting, grinding, casting, molders, platers)—brain or other CNS tumor
Thomas et al. 1986	U.S.	Case control	47	2.1	1.2, 3.6	Usual occupation of precision metal worker—brain or other CNS tumor
			26	1.8	0.9, 3.7	Usual occupation as machinist—brain or other CNS tumor
			7	1.8	0.5, 7.4	Usual occupation as tool and die maker— brain or other CNS tumor

See footnotes at end of table.

(Continued)

Table 5–13 (Continued). Brain/nervous system cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population and cancer site or cell type
Population-based studies (continued):						
Thomas et al. 1987	U.S.	Case control	49	1.6	1.0, 2.6	Ever employed at a job with potential cutting oil exposure—astrocytoma

*Abbreviations: CI=confidence interval, PMR=proportionate mortality ratio, NA=not available, NS=not statistically significant, SMR=standardized mortality ratio.
†Numbers were too small to calculate.

Table 5–14. Prostate cancer results from epidemiologic studies of MWF-exposed populations

Authors	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI* or *P*-value	Study population
Cohort studies:						
Decoufle 1978	Michigan	SMR	6	0.57	NS	White
			3	0.58	NS	White, 5+ yr of heavy oil mist exposure
Järvholm and Lavenius 1987	Sweden	SIR	6	0.34	0.1, 0.7	Grinders and turners
			6	0.38	0.1, 0.8	Grinders and turners, at least 20 yr since onset of exposure
Rotimi et al. 1993	Ohio	SMR	8	0.87	0.37, 1.70	Engine plant workers, white
			5	1.29	0.41, 3.00	Engine plant workers, black
Tolbert et al. 1992	Michigan	SMR	72	1.16	0.91, 1.46	Ever exposed to straight oil, white
			125	1.08	0.90, 1.28	Ever exposed to soluble oil, white
			26	1.11	0.73, 1.63	Ever exposed to synthetic oil, white
			12	0.98	0.51, 1.72	Ever exposed to straight oil, black
			23	0.98	0.62, 1.47	Ever exposed to soluble oil, black
Proportionate mortality studies:						
Mallin et al. 1986	Illinois	PMR	10	1.53	NS	White

(Continued)

*Abbreviations: CI=confidence interval, MOR=mortality odds ratio, PMR=proportionate mortality ratio, NS=not statistically significant, SIR=standardized incidence ratio, SMR=standardized mortality ratio.

Table 5–14 (Continued). Prostate cancer results from epidemiologic studies of MWF-exposed populations

Authors	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population
Proportionate mortality studies (continued):						
Park and Mirer 1996	Detroit area	PMR	8	1.08	0.47, 2.13	Engine Plant 1 workers, white
			19	1.61	1.03, 2.50	Engine Plant 2 workers, white
		MOR	4	4.52	1.43, 14.3	Tool grinders
		MOR	3	4.51	1.22, 16.6	Workers machining aluminum pistons
Park et al. 1988	Connecticut	PMR	10	0.92	0.50, 1.69	White
Proportionate mortality studies:						
Silverstein et al. 1988	Connecticut	PMR	29	1.00	0.70, 1.43	White
Vena et al. 1985	New York	PMR	7	1.06	NS	Based on U.S. mortality, white
			2	0.72	NS	Employed in engine plant >20 yr
Population-based studies:						
Aronson et al. 1996	Montreal	Case control	58	1.40	1.00, 1.97	Workers with substantial exposure to lubricating oils and greases
Siemiatycki et al. 1987	Montreal	Case control	47	1.2	90% CI: 1.0, 1.6	Ever exposed to cutting oils

Table 5-15. Lung/respiratory system cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI* or *P*-value	Study population and cancer site or cell type
Cohort studies:						
Acquavella et al. 1993	Iowa	SMR	42	1.3	0.9, 1.8	Total workforce
			18	2.2	1.3, 3.4	Factory workers employed >10 yr and hired between 1950 and 1959
Eisen et al. 1992	Michigan	SMR	60	0.91	0.70, 1.17	White auto workers in Plant III
Järvholm and Lavenius 1987	Sweden	SIR	5	0.40	0.1, 0.9	Grinders and turners
			3	0.30	0.1, 0.9	Grinders and turners, at least 20 yr since onset of exposure
Rotimi et al. 1993	Ohio	SMR	81	1.20	0.95, 1.40	Engine plant workers, white
			23	1.35	0.85, 2.02	Engine plant workers, black
Schroeder et al. 1997	Michigan	Nested case control	40	0.56	0.38, 0.82	Workers with highest exposure to synthetic MWFs
Tolbert et al. 1992	Michigan	SMR	251	1.02	0.90, 1.15	Ever exposed to straight oil, white
			478	1.07	0.97, 1.17	Ever exposed to soluble oil, white
			116	1.01	0.83, 1.21	Ever exposed to synthetic oil, white
			35	1.06	0.74, 1.48	Ever exposed to straight oil, black
			64	0.91	0.70, 1.17	Ever exposed to soluble oil, black

(Continued)

*Abbreviations: CI=confidence interval, MOR=mortality odds ratio, PMR=proportionate mortality ratio, NA=not available, NS=not statistically significant, SIR=standardized incidence ratio, SMR=standardized mortality ratio.

Table 5-15 (Continued). Lung/respiratory system cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population and cancer site or cell type
Proportionate mortality studies:						
Mallin et al. 1986	Illinois	PMR	34	1.27	NS	White
			12	1.29	NS	Black
Park and Mirer 1996	Detroit area	PMR	33	0.83	0.60, 1.15	Engine Plant 1 workers, white
			81	1.23	1.00, 1.52	Engine Plant 2 workers, white
		MOR	Not reported	0.89	0.67, 1.2	Workers grinding with soluble MWF
Park et al. 1988	Connecticut	PMR	59	1.23	0.96, 1.57	White men—both primary and secondary lung cancer
		Case control	5	19.3	*P*=0.008	Women ever employed in grinding
Silverstein et al. 1988	Connecticut	PMR	83	0.92	0.75, 1.13	White—both primary and secondary lung cancer
			13	0.62	NS	Workers employed in grinding 10 yr or more
Vena et al. 1985	New York	PMR	48	1.25	NS	Based on U.S. mortality, white
			29	1.40	NS	Employed in engine plant >20 yr

(Continued)

Table 5-15 (Continued). Lung/respiratory system cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population and cancer site or cell type
Population-based studies:						
Coggon et al. 1984	Britain	Case control	113	1.4	1.1, 1.8	Ever had an occupation with potential MWF exposure
			25	1.0	0.6, 1.6	Ever had an occupation with potentially high MWF exposure
Jöckel et al. 1992	Germany	Case control	NA	2.2	1.05, 4.75	Employed 6 months or more as a turner, grinder, driller, or cutter
Siemiatycki et al. 1987	Montreal	Case control	23	1.5	90% CI: 1.0, 2.1	Ever exposed to cutting oils—oat cell cancer of the lung
Other:						
Park et al. 1994	Ohio	MOR	4	1.64	0.56, 4.8	Ever employed as tool and die worker

Table 5-16. Colon cancer from results epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI* or *P*-value	Study population
Cohort studies:						
Acquavella et al. 1993	Iowa	SMR	1	0.1	0, 0.5	Total workforce
Decoufle 1978	Michigan	SMR	17	1.3	NS	White
			7	1.1	NS	White, 5+ yr of heavy oil mist exposure
Eisen et al. 1992	Michigan	SMR	22	1.47	0.92, 2.22	White auto workers in Plant III
Tolbert et al. 1992	Michigan	SMR	59	0.79	0.61, 1.03	Ever exposed to straight oil, white
			116	0.85	0.70, 1.02	Ever exposed to soluble oil,white
			26	0.83	0.54, 1.22	Ever exposed to synthetic oil, white
			3	0.42	0.08, 1.23	Ever exposed to straight oil, black
			8	0.55	0.24, 1.09	Ever exposed to soluble oil, black
Proportionate mortality studies:						
Mallin et al. 1986	Illinois	PMR	10	1.17	NS	White
			2	1.04	NS	Black
Park et al. 1988	Connecticut	PMR	15	1.18	0.71, 1.94	White
Silverstein et al. 1988	Connecticut	PMR	41	1.39	1.03, 1.88	White
			13	1.89	*P*=0.02	Employed in grinding 10 yr or more
Vena et al. 1985	New York	PMR	14	1.49	NS	Based on U.S. mortality, white
			8	1.70	NS	Employed in engine plant >20 yr

(Continued)

*Abbreviations: CI=confidence interval, PMR=proportionate mortality ratio, NS=not statistically significant, SMR=standardized mortality ratio.

Table 5-16 (Continued). Colon cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population
Population-based studies:						
Gerhardsson de Verdier et al. 1992	Sweden	Case control	25	1.5	0.8, 2.8	Ever exposed to cutting fluids
Siemiatycki et al. 1987	Montreal	Case control	32	1.0	90% CI: 0.8, 1.4	Ever exposed to cutting oils

Table 5-17. Hematopoietic and lymphopoietic cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI* or *P*-value	Study population and cancer site
Cohort studies:						
Decoufle 1978	Michigan	SMR	3	0.56	NS	White—leukemia
			2	0.76	NS	White, 5+ yr of heavy oil mist exposure—leukemia
Eisen et al. 1992	Michigan	SMR	9	1.07	0.49, 2.02	White auto workers in Plant III—leukemia
Tolbert et al. 1992	Michigan	SMR	38	1.25	0.88, 1.71	Ever exposed to straight oil, white— leukemia
			75	1.33	1.05, 1.67	Ever exposed to soluble oil, white— leukemia
			16	1.22	0.70, 1.98	Ever exposed to synthetic oil, white—leukemia
			2	0.55	0.22, 1.13	Ever exposed to straight oil, black—leukemia
			4	0.74	0.20, 1.90	Ever exposed to soluble oil, black— leukemia

See footnotes at end of table.

(Continued)

Table 5-17 (Continued). Hematopoietic and lymphopoietic cancer results from epidemiologic studies of MWF-exposed populations

Autor	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population and cancer site
Proportionate mortality studies:						
Mallin et al. 1986	Illinois	PMR	8	1.19	NS	White—lymphatic and hematopoietic
			3	1.36	NS	White—non-Hodgkin's lymphoma
			1	0.38	NS	White—leukemia
			6	3.54	*P*<0.01	Black—lymphatic and hematopoietic
			3	6.87	*P*<0.05	Black—non-Hodgkin's lymphoma
			1	†		Black—leukemia
Park and Mirer 1996	Detroit area	PMR	4	1.03	0.28, 2.63	Engine Plant 1 workers, white—non-Hodgkin's lymphoma and multiple myeloma
			6	0.95	0.35, 2.08	Engine Plant 2 workers, white—non-Hodgkin's lymphoma and multiple myeloma
		MOR	7	4.12	1.10, 15.4	Workers machining with soluble MWF—non-Hodgkin's lymphoma and multiple myeloma

See footnotes at end of table.

(Continued)

Table 5-17 (Continued). Hematopoietic and lymphopoietic cancer results from epidemiologic studies of MWF-exposed populations

Author	Location	Type of study/ analysis	Number with cancer or number of exposed cases	Rate ratio	95% CI or *P*-value	Study population and cancer site
Proportionate mortality studies (continued):						
Park et al. 1988	Connecticut	PMR	7	0.60	0.29, 1.23	White—all lymphopoietic cancer
			1	0.23	0.01, 1.26	White—leukemia
Silverstein et al. 1988	Connecticut	PMR	27	1.03	0.71, 1.50	White—all lymphopoietic cancer
			12	1.10	0.63, 1.94	White—leukemia
			5	0.84	NS	Employed in grinding 10 yr or more—all lymphopoietic cancer
Vena et al. 1985	New York	PMR	8	0.86	NS	Based on U.S. mortality, white—lymphatic and hematopoietic
			4	0.85	NS	Employed in engine plant >20 yr—lymphatic and hematopoietic
Population-based studies:						
Siemiatycki et al. 1987	Montreal	Case control	22	1.3	90% CI: 0.9, 1.8	Ever exposed to cutting oils—non-Hodgkin's lymphoma
Other:						
Park et al. 1994	Ohio	MOR	3	5.38	1.6, 18	Ever employed as tool and die worker

*Abbreviations: CI=confidence interval, MOR=mortality odds ratio, PMR=proportionate mortality ratio, NS=not statistically significant, SMR=standardized mortality ratio.
†Numbers were too small to calculate.

expected, a significantly elevated risk was not observed in the one cohort mortality study that reported skin cancer mortality (Table 5–6).

PMR studies

Again, as would be expected, a significantly elevated risk was not observed in any of the three PMR studies that reported skin cancer mortality (Table 5–6).

Population-based studies

In a population-based case-control study in Connecticut involving 45 cases of squamous cell carcinoma of the scrotum, those ever employed in an occupation potentially exposed to MWFs (toolmaker, setter, set-up man, hardener, polisher, automatic screw operator, machinist, and machine operator) had an increased risk for this cancer (OR=10.5, 95% CI=4.0–36.9) [Roush et al. 1982].

Conclusion for skin cancer

In conclusion, the large number of case reports, the cancer incidence study, and the case-control study suggest that primarily straight MWF exposure is associated with an increased risk for skin and scrotal cancer. However, as a result of the changes in MWF composition and reduction of impurities over the last several decades, current exposures to straight MWFs may be associated with a substantially reduced risk for scrotal and skin cancer.

5.3.3.2 Laryngeal Cancer

Cohort studies

Only the three automobile manufacturing plants studies conducted by Eisen et al. [1992] and Tolbert et al. [1992] reported site-specific data for laryngeal cancer (Table 5–7). Tolbert et al. [1992] reported a statistically significant standardized mortality ratio (SMR) of 1.98 for laryngeal cancer among whites ever exposed to straight oil, and a nearly significant SMR of 1.41 for soluble oil exposure in Plants I and II combined. The SMR for laryngeal cancer in Plant 3 was not elevated [Eisen et al. 1992]. In a case-control analysis including all three plants and incident as well as deceased cases, a categorized exposure analysis found an OR of 2.23 (95% CI=1.25–3.98) among individuals with >0.5 mg/m^3-years of straight oil particulate exposure. Eisen et al. [1994] also examined the association between laryngeal cancer and specific components or contaminants of MWFs (biocides, steel, iron, aluminum, sulfur, and chlorine). There was some evidence for confounding by sulfur, but models including both exposure variables still had a significantly elevated OR in the highest straight MWF exposure category (OR=1.91, 95% CI=1.01–3.62). Although unable to adjust for smoking and alcohol (two important risk factors for laryngeal cancer) Austin [1982] did not think that these risk factors confounded the results. The author found that the risk of lung cancer and

cirrhosis did not increase with increasing exposure to straight MWFs, suggesting that an association did not exist between straight oil exposure and cigarette smoking or alcohol use.

PMR studies

Among the three PMR studies reporting site-specific results for larynx cancer, the overall PMRs ranged from 1.7 to 1.8 [Park and Mirer 1996; Vena et al. 1985; Mallin et al. 1986]. In the Vena et al. [1985] study, a significantly elevated PMR was found for workers employed less than 20 years and those who were employed after 1950 (PMR=3.95, $P<0.05$ for both subgroups).

Population-based studies

Of six studies that defined occupational categories in sufficient detail to examine risk associated with exposure to MWF, one found a significant risk for "ever employment as a machinist" (SMR=2.5, 95% CI=1.2–5.2) or metal grinder (SMR=2.1, 95% CI=1.0–4.7) after adjustment for smoking and alcohol [Zagraniski et al. 1986]. A case-control study (hospital-based) of 100 laryngeal cancer cases and 100 controls found a nonsignificantly elevated risk among those who self-reported ever having mineral oil exposure (OR=2.2, 95% CI=0.9–5.3, adjusted for smoking and alcohol) [Ahrens et al. 1991]. One other study found an elevation in laryngeal cancer risk among workers with potential MWF exposure; however, this study did not control for smoking or alcohol consumption [Russi et al. 1997].

Conclusion for laryngeal cancer

In conclusion, several studies suggest that MWF exposure may be associated with laryngeal cancer. In particular, the studies by Eisen et al. [1992, 1994] and Tolbert et al. [1992] suggest that laryngeal cancer is associated with exposure to straight oil MWFs.

5.3.3.3 Rectal Cancer

Cohort studies

Aside from the three automobile manufacturing plant studies conducted by Eisen et al. [1992] and Tolbert et al. [1992], only one cohort study has reported site-specific results for rectal cancer [Decoufle 1978] (Table 5–8). Tolbert et al. [1992] reported an association between straight oil exposure and rectal cancer among white but not black workers. The SMR for ever-exposure to straight MWFs among whites was 1.47 (95% CI=1.04–2.03). Poisson regression analyses revealed a trend of increasing rectal cancer risk in relation to years of exposure to straight MWFs ($P<0.0001$). The RR for the most highly exposed group was 3.2 (95% CI=1.6–6.2). Plant III had a nonsignificant excess (SMR=1.70) [Eisen et al. 1992]. The Decoufle [1978] study found a slight excess of rectal cancer mortality that was not statistically significant.

PMR studies

Among the four PMR studies reporting data for rectal cancer, one found a significant excess in the cohort with potential exposure to straight and soluble oil MWFs (PMR=3.07, 95% CI=1.54–5.50) [Park et al. 1988]. Park et al. [1988] did not report the risk for each specific type of MWF exposure. A second PMR study found a significant excess in a subgroup with employment in an engine plant for >20 years (PMR=2.76, $P<0.05$) (although all three types of MWF were used at this plant, their temporal use was not known to the study investigators) [Vena et al. 1985]. Silverstein et al. [1988] found a slight excess of rectal cancer mortality, which was not statistically significant; the risk for various processes was not reported. Mallin et al. [1986] found a risk of <1; however this finding is based on only two rectal cancer deaths.

Population-based studies

A population-based case-control study of incident cases of rectal cancer in Sweden found that male workers ever exposed to cutting fluids had an elevated risk for rectal cancer (OR=2.1, 95% CI=1.1–4.0) [Gerhardsson de Verdier et al. 1992]. However, several of the cases had other occupational exposures that have been associated with an increased risk for rectal cancer—including exposure to asbestos, soot, and combustion gases from coal/coke/wood. In an analysis adjusting for these other exposures, the risk of rectal cancer among cutting-oil-exposed workers was lower (OR=1.4, 95% CI= 0.6–3.5). In another population-based case-control study that examined the association between several cancer sites and occupational exposure to several petroleum-derived liquids, ever having cutting oil exposure was found not to be associated with an increased risk for rectal cancer (OR=0.7, 90% CI=0.4–1.0) [Siemiatycki et al.1987].

Conclusions for rectal cancer

In conclusion, several studies suggest that MWF exposure is associated with rectal cancer. In particular, the findings from the study with the most statistical power suggest that straight oil exposure may be associated with an increased risk for rectal cancer [Tolbert et al. 1992].

5.3.3.4 Pancreatic Cancer

Cohort studies

Among five cohort studies reporting site-specific data for pancreatic cancer, one found a significant excess for black but not white workers [Rotimi et al. 1993], and one found a significant excess for white workers in a subgroup analysis [Acquavella et al. 1993] (Table 5–9). Rotimi et al. [1993] found that black men employed at two Ohio engine manufacturing plants had an excess pancreatic cancer mortality (SMR=3.03, 95% CI=1.21–6.24, based on 7 deaths). However, it should be noted that the authors found no consistent pattern with respect to time since hire or duration of employment, and no pancreatic cancer excess was observed in white workers. Acquavella et al. [1993] reported

that factory workers employed at an Iowa metalworking facility had an increased risk for pancreatic cancer mortality (SMR=2.0, 95% CI=0.9–3.8). The risk appeared to be greatest among factory workers employed 10 or more years who were hired between 1950 and 1959 (SMR=3.6, 95% CI=1.2–8.3); however, the authors did not report whether a specific occupational group was responsible for the elevation identified in this subcohort. Among those in the overall cohort, assembly workers—who (Acquavella et al. state) are unlikely to have MWF exposure—were the occupational group with the highest risk (SMR=3.0, 95% CI=1.0–7.5). By contrast, in those departments identified by Acquavella et al. as having potential MWF exposure, there were 2 observed pancreatic cancer deaths in the overall cohort whereas 3.3 deaths were expected. Tolbert et al. [1992] found excess pancreatic cancer mortality among black workers exposed to soluble MWFs at Plants I and II in Michigan (SMR=1.62, 95% CI=0.98–2.54). In a Poisson regression analysis that controlled for race, age, and gender, an increased risk for pancreatic cancer mortality was observed in those workers with the highest exposures to synthetic MWFs (RR=2.04, 95% CI=0.88–4.72) [Tolbert et al. 1992]. In a case-control analysis that included Plants I, II, and III, a categorized exposure analysis found an OR of 2.23 (95% CI=1.25–3.98) among workers with >1.4 mg/m^3-years grinding with synthetic MWF [Bardin et al. 1997]. However, neither synthetic MWF nor any other measured exposure was found to explain the previously documented excess pancreatic cancer risk among black workers [Bardin et al. 1997]. Although unable to adjust for smoking, an important risk factor for pancreatic cancer [Silverman et al. 1994], Bardin et al. did not think that this risk factor confounded their results because the risk of lung cancer did not increase with increasing exposure to synthetic MWFs. One other cohort study found a nonsignificant elevation in pancreatic cancer mortality; however, this study had limited statistical power [Decoufle 1978].

PMR studies

Among five studies reporting site-specific data for pancreatic cancer, one found a significantly elevated PMR among white workers [Vena et al. 1985], one found a significantly elevated PMR among black but not white workers [Mallin et al. 1986], and two found significantly elevated PMRs among workers machining with straight oil MWF [Silverstein et al. 1988; Park and Mirer 1996]. White men employed at an engine plant for at least 10 years had an excess of pancreatic cancer mortality (PMR=1.89, $P<0.05$), which was higher for those employed more than 20 years (PMR=2.32, $P<0.05$) [Vena et al. 1985]. Use of county referent rates resulted in higher PMRs (employed >10 years, PMR=2.41, $P<0.05$; employed >20 years, PMR=2.97, $P<0.05$). PMRs for nonwhites employed in the engine plants were not reported because of the small numbers of deaths. All three types of cutting fluids were used in the engine plants. Mallin et al. [1986] found a significant excess of pancreatic cancer among black (PMR=3.57, $P<0.05$) but not white (1.19, n.s.) men employed in the manufacture of diesel engines and construction equipment. The PMR for pancreatic cancer was highest among black men who died after 20 years of service (PMR=4.79, $P<0.01$). Another PMR study found an elevation

in pancreatic cancer mortality among whites at a ball-bearing manufacturing plant (PMR=1.43, 95% CI=0.96–2.12) [Silverstein et al. 1988]. Case-control analyses revealed substantially elevated risks associated with 10 or more years of employment in grinding with various MWFs (OR=3.10, P=0.05) and machining with straight oil MWF (OR=5.31, P=0.05). The risk associated with grinding was present only for those with early hire dates (in the early 1930s and before) when straight oil MWFs were "almost exclusively used in grinding." Too few deaths occurred among non-white men for analysis. A PMR study of workers at two engine plants did not observe significant excesses for pancreatic cancer [Park and Mirer 1996]. However, an MOR analysis of these workers found an increased risk among those ever employed in machining with straight oil MWFs (OR=3.61, 95% CI=1.04–12.6, based on 3 cases); but no trend was observed with increasing cumulative exposure. One other PMR study found a nonsignificant elevation in pancreatic cancer mortality; however, a mortality odds ratio (MOR) analysis was not reported [Park et al. 1988].

Population-based studies

One study of white males in Los Angeles county during the period 1972–77 reported a nonsignificant "proportional index ratio" for employment as a machinist [Mack and Paganini-Hill 1981].

Conclusion for pancreatic cancer

In conclusion, several studies have found significantly increased risks of pancreatic cancer among workers exposed to MWF. The evidence is strongest for grinding with synthetic MWF [Bardin et al. 1997] and for machining with straight oil MWFs [Silverstein et al. 1988; Park and Mirer 1996]. Although a number of the studies did not have internally consistent findings (i.e., excesses in black but not white workers, lack of association with duration of MWF exposure), the number of studies with statistically significant findings suggests that exposure to some MWFs may increase the risk of pancreatic cancer.

5.3.3.5 Bladder cancer

Cohort studies

Only two cohort studies reported site-specific data for bladder cancer and neither found a significant excess [Decoufle 1978; Järvholm and Lavenius 1987] (Table 5–10). However, both of these studies are limited by relatively small sample sizes.

PMR studies

Of the six PMR studies that reported site-specific data for bladder cancer, only one reported a significant excess (PMR=2.28, P<0.05), which was among white workers employed in an engine plant [Vena et al. 1985]. The risk was greatest among those first employed during or before 1950 (PMR=3.37, P<0.05). A study of bearing plant

workers also found a nonsignificantly elevated risk for bladder cancer [Silverstein et al. 1988]. Another PMR study of workers at two Detroit-area engine manufacturing plants found nonsignificantly elevated PMRs for bladder cancer [Park et al. 1996]. However, a mortality OR analysis of these workers found a significant association between risk for bladder cancer and cumulative exposures to grinding with straight oil (MOR for the mean cumulative exposure of exposed cases=2.99, 95% CI=1.15–7.77, based on 7 deaths), and in the machining or heat-treat area (MOR for the mean cumulative exposure of exposed cases=2.86, 95% CI=1.14–7.18 based on 4 deaths). Two studies did not find an increased risk for bladder cancer [Park et al. 1988; Mallin et al. 1986], however these studies are limited by small sample size.

Population-based studies

Several case-control studies have also examined the risk of bladder cancer among those whose occupations may involve MWF exposure. Only those studies that controlled for smoking (a known risk factor for bladder cancer [Matanoski and Elliott 1981]) are discussed in detail. In a large population-based case-control study from the United States, Silverman et al. [1989a] found an elevated risk for bladder cancer among white men ever employed as machinists (OR=1.3, 95% CI=1.0–1.7) or drill press operators (OR=1.4, 95% CI=0.9–2.1). Furthermore, among drill press operators, the risk increased with increasing duration of employment (*P* for trend=0.008). Among drill press operators who worked 5 or more years, the elevated risk was present in both those who began work before 1950 (OR=1.7, confidence limits not provided) and those who began work in 1950 or later (OR=2.9, confidence limits not provided). However, among those who were employed as drill press operators for less than 5 years, the risk for bladder cancer was increased only among those who began employment in 1950 or later (OR=2.8, confidence limits not provided). The same study [Silverman et al. 1989b] examined occupational risk factors for bladder cancer among nonwhite men and reported an RR of 1.1 (95% CI=0.6–1.9) for the summary category *metal machinery worker* which was identical to the summary category *metal machinery worker* for whites (RR=1.1, 95% CI=1.0–1.3). The risks for the subcategories *machinists* and *drill press operators* was not broken out for nonwhites, nor was duration of employment as a metal machinery worker examined. In a population-based case-control study from Canada, Howe et al. [1980] found that those ever employed as metal machinists had an increased risk for bladder cancer (OR=2.7, 95% CI=1.1–7.7). A hospital-based case-control study conducted in Germany found that individuals ever employed as turners had an increased risk for bladder cancer (OR=2.25, 95% CI=1.0–5.6), and the risk was consistently elevated with increasing duration of employment (*P* for trend=0.08) [Claude et al. 1988]. This same study also found no increased risk of bladder cancer for the broad category of metal workers (OR=0.84, 95% CI=0.54–1.3). A population-based case-control study from Belgium found that metalworkers had a significantly increased risk for bladder cancer (RR=2.45, 95% CI=1.28–4.69). Subgroup analyses of these workers found the highest risk among turners (RR=2.57, 95% CI=0.92–7.16) [Schifflers et al. 1987].

Another hospital-based case-control study from Italy found that those employed for 6 months or more in the machine-tool industry had an increased risk for bladder cancer (OR=1.5, 95% CI=0.7–3.3) [Vineis and Magnani 1985]. Within the machine-tool trade, the risk for bladder cancer was elevated among turners, especially among turners hired before 1940 and employed more than 10 years (RR=3.1, 95% CI=0.9–10.5). A population-based case-control study conducted in Hamilton County, Ohio, found that grinding machine operators had an increased risk for bladder cancer (OR=2.00, not significant), whereas machinists were found to have a significantly decreased risk (OR=0.69) [Steenland et al. 1987]. Another case-control study did not observe an increased risk for bladder cancer among toolmakers (RR=0.77, 95% CI=0.5–1.1) but did observe an increased risk among machinery adjusters, assemblers, and mechanics (RR=1.86, 95% CI=1.2–2.8) [Gonzalez et al. 1989]. Four other studies found an elevation in bladder cancer risk among workers with potential MWF exposure; however, none of these four studies controlled for smoking [Malker et al. 1987; Coggon et al. 1984; Tola et al. 1980; Dunham et al. 1968].

Conclusions for bladder cancer

In summary, the association between bladder cancer and MWF exposure is well supported by one large and well designed case-control study [Silverman et al. 1989a, b] as well as several other studies conducted in different geographic locations, all of which controlled for smoking. Although none of the cohort studies found a significantly increased risk for bladder cancer, it has been observed that mortality studies may not be suitable for detecting elevated risks for cancers with high survival rates [Schulte et al. 1985; Steenland et al. 1988].

5.3.3.6 Stomach Cancer

Cohort studies

Only one of six cohort studies found a significantly elevated risk for stomach cancer [Rotimi et al. 1993] (Table 5–11). Rotimi et al. [1993] found that stomach cancer mortality was increased among white hourly workers employed at two Ohio engine manufacturing plants (SMR=2.54, 95% CI=1.42–4.20). Using local mortality rates to account for a high proportion of foreign-born workers, the magnitude of association decreased but the SMR for stomach cancer remained significantly elevated and displayed a dose-response relationship with duration of exposure (SMR not provided). Most of the excess in this cohort occurred among those hired before 1955 with 20 or more years since first hire who were employed for 20 or more years. However, the findings from this study should be interpreted cautiously because of limitations identified by the study authors (i.e., limited work history information and lack of data on possible confounding factors such as country of birth and previous employment history.

The Tolbert [1992] and Eisen studies [1992] (the largest and best designed of the cohort studies) did not observe a significant elevation in stomach cancer mortality. Nonsignificant elevations in stomach cancer mortality for white workers were observed in two of the three study plants (Plant 1: SMR=1.08, 95% CI=0.84–1.36); Plant 2: SMR=1.26, 95% CI=0.87–1.77; Plant 3: SMR=0.59, 95% CI=0.16–1.50) [Eisen et al. 1992]. Black men did not have an elevated SMR for stomach cancer associated with either employment at Plant 1 (SMR=0.96, 95% CI=0.56–1.54) or exposure to straight or soluble oil MWFs. Analysis of risks associated with specific fluid types (Table 5–11) indicated slight excesses of stomach cancer in each of the exposure groups. Poisson modeling did not suggest strong exposure-response trends for any of the 3 exposure types, although there was a slight elevation in the highest exposure group for soluble MWFs relative to other strata [Tolbert et al. 1992]. Tolbert et al. [1992] concluded that "the results of the Poisson analysis were not inconsistent with a dose-response relationship between soluble machining fluid and stomach cancer risk." The three other cohort studies found nonsignificant elevations in stomach cancer mortality [Acquavella et al. 1993; Järvholm and Lavenius 1987; Decoufle 1978], two of which were limited by low statistical power [Acquavella et al. 1993; Järvholm and Lavenius 1987].

PMR studies

Three of five PMR studies found a significantly elevated risk for stomach cancer [Silverstein et al. 1988; Park et al. 1988; Park and Mirer 1996]. Silverstein et al. [1988] found that white men employed 5 or more years in a ball-bearing manufacturing plant had an elevated risk for stomach cancer mortality (PMR=1.97, $P<0.001$). The risk was greatest among white men with 10 or more years employment in grinding operations that used primarily soluble MWFs (PMR=3.39, $P<0.001$); this risk was not found among machinists who used straight MWFs. The association with grinding persisted even after adjusting for Central European origin using logistic regression. Silverstein et al. [1988] concluded that their study provided strong evidence that grinding operations using soluble cutting fluids increase the risk for stomach cancer. White men employed in grinding operations at another ball-bearing manufacturing plant were also found to have excess stomach cancer mortality (PMR=3.8, $P=0.006$) [Park et al. 1988]. Workers classified as having soluble oil MWF exposure in a nested case-control analysis were found to have an OR for stomach cancer of 6.2 ($P=0.05$) [Park et al. 1988]. In interpreting these findings Park et al. did not think that there was confounding by the Central European origin of the workers because they found no association between such origin and soluble oil exposure. Another PMR study of workers at two Detroit-area engine manufacturing plants did not find an elevated PMR for stomach cancer at either plant [Park and Mirer 1996]. However, an MOR analysis of these workers found a significant association between risk for stomach cancer and duration of employment in camshaft/crankshaft production at Plant 1 (MOR for the mean employment duration of exposed cases=5.1, 95% CI=1.6–17, based on three deaths), but not at the larger and older Plant 2 (MOR not provided). Workers involved in camshaft/crankshaft production at

Plant 1 were reported to have exposure to semisynthetic MWFs and nitrosamines. Why a similar excess risk was not found in Plant 2 is not clear. Furthermore, this study found no association between stomach cancer and grinding with either soluble oil MWF (MOR=0.91) or straight oil MWF (MOR=0.61). Two other PMR studies found nonsignificant elevations in stomach cancer mortality [Vena et al. 1985; Mallin et al. 1986]; these two studies were limited by low statistical power.

Population-based studies

One of three population-based studies found a significant association between working in an occupation with potential MWF exposure and risk of stomach cancer [Kneller et al. 1990]. A standardized incidence ratio (SIR) study of incident stomach cancer cases reported to the Shanghai, China, Cancer Registry found that men with a current occupation of metal grinder, polisher, tool sharpener, or machine-tool operator had an elevated risk for stomach cancer (SIR=1.41, $P<0.01$) [Kneller et al. 1990].

Other studies

Park et al. [1994] found a significantly increased MOR (9.65, 95% CI=2.3–40) among tool and die workers exposed to MWFs at a stamping plant within the automobile industry. It should be noted that this finding is based on only two stomach cancer deaths.

Conclusions for stomach cancer

In conclusion, limited evidence supports an association between MWF exposure and stomach cancer. The association between stomach cancer and MWF exposure is supported by one cohort study and three PMR/MOR studies. However, the largest and best designed cohort study provides little support for an association [Tolbert et al. 1992; Eisen et al. 1992]. The findings from Park et al. [1988] and Silverstein et al. [1988] suggest that grinding operations using soluble oil MWF may be associated with an elevated risk for stomach cancer.

5.3.3.7 Esophageal Cancer

Cohort studies

Among four cohort studies that reported site-specific results for this cancer, none found a significant excess in the overall analyses (Table 5–12). With Poisson regression analyses, Tolbert et al. [1992] found elevations in esophageal cancer risk among those with straight MWF exposure and synthetic MWF exposure; however, clear dose-response trends were not present.

PMR studies

One of four PMR studies reported a significant excess [Silverstein et al. 1988]. Silverstein et al. [1988] found a PMR of 1.83 for esophageal cancer among MWF-exposed workers (95% CI=1.07–3.12). No further analysis by exposure or job category was

performed by Silverstein et al. [1988]. The other three PMR studies are limited by small numbers of esophageal cancer deaths.

Conclusions

In conclusion, limited evidence exists for an association between esophageal cancer and MWF exposure.

5.3.3.8 Other Sites

Other sites: Equivocal evidence exists regarding the potential association of MWF exposure with cancer of the brain and nervous system, prostate, lung/respiratory system, colon and hematopoietic and lymphopoietic systems (Tables 5–13 through 5–17) and are only briefly summarized here.

5.3.3.9 Brain/Nervous System Cancer

Among three cohort studies that reported site-specific results for brain/nervous system cancer, none found a significant excess (Table 5–13). Tolbert et al. [1992] reported a nearly significant association with soluble oil exposure among whites (SMR=1.24, 95% CI=0.91–1.66); however, Poisson regression analysis found no dose-response trend with soluble oil exposure. None of five PMR studies that reported results for brain/nervous system cancer found a significant elevation. A case-control study using death certificate data to classify occupation reported a significant association between all brain cancers and *usual occupation of precision metal worker* (OR=2.1, 95% CI=1.2–3.6) [Thomas et al. 1986]. An case-control interview study of astrocytic brain tumors (including cases identified in the Thomas et al. [1986] study) reported an OR of 1.6 (95% CI=1.0–2.6) for *ever employed at a job with potential cutting oil exposure* [Thomas et al. 1987].

5.3.3.10 Prostate Cancer

Among four cohort studies that reported site-specific results for prostate cancer, none showed a significant excess in the overall analyses (Table 5–14). Tolbert et al. [1992] observed slight excesses for each exposure group among the white males and a mild exposure-response trend for exposure to straight machining fluid (P=0.03). The rate ratio for ≥7.5 years of straight oil machining fluid exposure was 1.5 (95% CI=1.01–2.29). One study found a significant deficit of prostate cancer among *grinders and turners* (SMR=0.34, 95% CI=0.1–0.7) and among *grinders and turners* with at least 20 years since onset of exposure (SMR=0.38, CI=0.1–0.8) [Järvholm and Lavenius 1987]. Among 5 PMR studies that reported site-specific results for prostate cancer, one showed a significant excess [Park and Mirer 1996]. Park and Mirer [1996] found that workers at one of two Detroit-area engine manufacturing plants had an elevated PMR for prostate cancer. The MOR analysis of workers at these two plants found that two activities with

potential MWF exposure were associated with an increased risk for prostate cancer: tool grinding and machining of aluminum pistons.

5.3.3.11 Lung Cancer

Of five cohort studies reporting site-specific results for lung cancer, only one reported a statistically significant increased risk, and this was for a subgroup of workers employed >10 years and hired between 1950 and 1959 [Acquavella et al. 1993] (Table 5–15). Some studies, in fact, provide evidence for a negative association between MWF exposure and lung cancer. Although the SMR analyses in the Tolbert et al. [1992] study showed SMRs >1.00 for workers ever exposed to each of three types of machining fluids, the Poisson regression analyses found a negative association between lung cancer risk and both synthetic MWF exposure (P=0.006), and soluble oil MWF exposure (P=0.09). Findings were similar in a case-control analysis that included all three plants [Schroeder et al. 1997]. Schroeder et al. [1997] suggested that the negative findings may be due to contamination of the water-based fluids by endotoxin-producing gram-negative bacteria. The mechanism proposed by these authors was that endotoxins may stimulate immunologic factors that inhibit the growth of malignant cells in the lung. However, these authors could not rule out other noncausal mechanisms (e.g., selective attrition of susceptible workers or inverse correlation between synthetic MWF exposure and exposure to an unmeasured occupational lung carcinogen). Järvholm and Lavenius [1987] also found that workers exposed to oil mist for 5 or more years had a significantly decreased risk for lung cancer (SMR=0.4, 95% CI=0.1–0.9), even among those with at least 20 years since onset of exposure (SIR=0.30, 95% CI=0.1–0.9) (Table 5–15). Four of five PMR studies report PMRs >1.0, one of which was statistically significant [Park and Mirer 1996]. The PMR study of workers at two Detroit-area engine manufacturing plants found an elevated PMR for lung cancer at only one of the plants [Park and Mirer 1996]. The MOR analysis of these workers did not provide clear evidence that the excess lung cancer risk was due to MWF exposure. A case-control study within a PMR study reported a significantly increased risk for female workers employed as grinders, but the absence of any cases in the comparison group made this an unstable estimate [Park et al. 1988]. Three population based case-control studies report statistically significant ORs associated with various definitions of MWF exposure [Siemiatycki et al. 1987; Jöckel et al. 1992; Coggan et al. 1984].

5.3.3.12 Colon Cancer

Among four cohort studies reporting site-specific data, none show significant excesses (Table 5–16). One of 4 PMR studies was significantly positive [Silverstein et al. 1988]. Silverstein et al. [1988] found a significant excess in colon cancer (PMR=1.39, 95% CI=1.03–1.88) that appeared to be concentrated in workers employed in grinding operations (13 observed, 6.9 expected, PMR=1.89, P=0.02). MOR analyses using logistic regression found no exposure associations for colon cancer.

5.3.3.13 Hematopoietic and Lymphopoietic Cancer

One of three cohort studies reporting data on hematopoietic and lymphopoietic cancers found a significantly increased risk (Table 5–17). Tolbert et al. [1992] found that white men ever exposed to soluble oil MWFs had an increased risk for leukemia (SMR=1.33, 95% CI=1.05–1.67), but Poisson regression models found no evidence for an association between leukemia and any class of MWF. Another SMR study found an elevated lymphopoietic cancer risk in a small subgroup (workers employed 1 or more months in the tool and die area of an automotive stamping plant) (MOR=5.38, 95% CI=1.6–18.0, based on three lymphopoietic cancer deaths) [Park et al. 1994]. Among five PMR studies, none found significantly elevated PMRs in the overall analyses. However, Park and Mirer [1996] found that workers who ever worked in grinding with soluble oil MWFs had an increased risk for non-Hodgkin's lymphoma and multiple myeloma (MOR=4.1, 95% CI=1.1–15). Silverstein et al. [1988] found that workers employed as tool grinders for 10 or more years had an increased risk for lymphopoietic cancer (PMR=4.75, P=0.02). Mallin et al. [1986] found an elevated risk for non-Hodgkin's lymphoma among black workers (PMR=6.87, P<0.05). In each of these three studies, the authors speculated that solvent exposure [Park and Mirer 1996; Silverstein et al. 1988; Mallin et al. 1986] or biocides [Park and Mirer 1996], rather than MWF fluid exposure, were likely to be responsible for the elevated risks. A population-based case-control study that examined the association between several cancer sites and occupational exposure to several petroleum-derived liquids found evidence suggesting a dose-response relationship between cutting oil exposure and an increased risk for non-Hodgkin's lymphoma (OR among those defined as substantially exposed=1.9, 90% CI=1.0–3.1) [Siemiatycki et al. 1987].

5.3.4 Genetic Effects

Only one epidemiologic study was identified that examined genotoxicity among workers exposed to MWF [Fuchs et al. 1995]. In a German study of 65 male metal workers exposed to synthetic MWFs in seven small-to medium-sized plants, those who worked in areas having a NDELA concentration greater than 500 ng/m^3 had a significantly elevated mean number of DNA strand breaks in mononuclear blood cells compared with workers employed in areas with less than 50 ng/m^3 NDELA (1.69 ± 0.34 workers in areas with greater than 500 ng/m^3 NDELA versus 0.76 ± 0.05 for workers in areas with less than 50 ng/m^3 NDELA, P<0.01) [Fuchs et al. 1995]. The average concentration of NDELA present in the cutting fluids at these plants was 20.6 ppm (range 2–135 ppm). In addition, nonsmokers who worked more than 4.5 hr/day had a significantly elevated mean number of DNA strand breaks compared with nonsmokers who worked less than 4.5 hr/day (1.34 ± 0.12 for those working more than 4.5 hr/day versus 0.91 ± 0.12 for those working less than 4.5 hr/day, P<0.02). Airborne concentrations of MWFs were not reported. NDELA is a contaminant that may be present in some MWFs and can be formed in MWFs when DEA or TEA reacts with a nitrosating agent (e.g., nitrite). This