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Mortality studies of machining-fluid exposure in the automobile industry. II. Risks associated with specific fluid types.

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Mortality studies of machining-fluid exposure in the automobile industry

II. Risks associated with specific fluid types

by Paige E Tolbert, PhD,¹ Ellen A Eisen, ScD,^{1,2} Lucille J Pothier, MS,¹ Richard R Monson, MD,¹ Marilyn F Hallock, MS,³ Thomas J Smith, PhD³

TOLBERT PE, EISEN EA, POTHIER LJ, MONSON RM, HALLOCK MF, SMITH TJ. Mortality studies of machining-fluid exposure in the automobile industry: II. risks associated with specific fluid types. *Scand J Work Environ Health* 1992;18:351-60. Excesses of digestive and respiratory cancers have been reported previously in association with exposure to machining fluids, agents in widespread use as coolants and lubricants in machining operations. Previous studies have had limited power to distinguish the effects of the different types of machining fluids in use. In a cohort of over 30 000 workers employed at two automotive plants in Michigan, mortality patterns were studied in relation to exposure to each of the three major fluid types — straight oils, soluble oils, and synthetic fluids. Standardized mortality ratios were estimated for subgroups of the cohort ever exposed to each of the three fluid types, and Poisson regression analyses were used to assess trends in risk with duration of exposure. The data suggest modest positive associations between exposure to straight oils and rectal, laryngeal, and prostatic cancer and a negative association between soluble and synthetic fluid exposure and lung cancer.

Key terms: cohort study, cutting oils, laryngeal cancer, lung cancer, metalworking, mineral oil, oil mists, polycyclic aromatic hydrocarbons, prostatic cancer, rectal cancer.

This is the second of a series of papers describing findings of a mortality investigation in a cohort exposed to machining fluids. The study was undertaken in response to reports of an association between digestive and respiratory cancers and exposure to machining fluids (1-7). Lifetime exposures of automotive manufacturing employees at three plants in Michigan are being studied in relation to cause-specific mortality. In our first report (8), a comparison of the mortality experience of the entire cohort to that of external reference populations (United States, state, and county) was presented. Excesses of leukemia and several cancers of a priori interest — cancers of the larynx, lung, stomach, and pancreas — were observed in the cohort as a whole. In this report, we present findings of a similar analysis for subgroups of the cohort defined on the basis of exposure to specific types of machining fluids. In addition, we present results of an internal analysis assessing trends in risk with duration of exposure, using Poisson regression.

Machining fluids encompass a diverse group of agents, and, to date, little effort has been directed toward distinguishing the effects of the various types of machining fluids. Rather than describing a specific chemical composition, the term machining fluid describes a function, that of cooling and lubricating surfaces in machining operations. Among suspect cancer initiators and promoters contained in one or another type of machining fluid as additives or contaminants are the following: long-chain aliphatics (9), polyaromatic hydrocarbons (10), nitrosamines (11, 12), sulfur-containing compounds (13), formaldehyde-releasing biocides (14), and certain metals (15). As part of the ongoing mortality study, an extensive exposure assessment involving review of historical records, interviews with plant personnel, and field measurements has been performed. This data base provided an opportunity to assess the effects of specific types of exposure.

For the present analysis, exposures to the following three major types of machining fluid were distinguished: straight, soluble, and synthetic fluids. Straight oils, also referred to as insoluble or cutting oils, are naphthenic or paraffinic mineral oils, with additives such as polar lubricants (eg, lard or sperm oil) and, occasionally, chlorine-, sulfur-, or phosphorus-based lubricants. Soluble oils, also called water-miscible or emulsified oils, are water-based oil emulsions with petroleum sulfonates or amine soaps to aid in droplet suspension. Additives include chlorine-, sulfur-, or phosphorus-based lubricants, corrosion inhibitors (eg, nitrites and polar organic compounds), chemical sta-

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bilizers (eg, complex alcohols and nonionic wetting agents), and biocides such as triazines. The third broad category of machining fluid is synthetic fluids, also referred to as chemical fluids. Containing no mineral oil, these are alkaline aqueous solutions of compounds such as ethanalamines. Agents added to synthetic fluids include corrosion inhibitors, surfactants, non-mineral oil lubricants such as silicones, and biocides. Whereas straight cutting oils have been in widespread use since the 19th century, soluble and synthetic fluids were introduced in the 1940s.

Our exposure assessment allowed identification of subgroups of subjects ever exposed to the three types of machining fluids — straight, soluble and synthetic fluids — and provided information on duration of exposure to the fluids. This paper presents the results of a standardized mortality analysis for these subgroups, as well as an internal analysis of trends in risk in relation to number of years of exposure to each fluid type.

Subjects and methods

Study population

The study base in the present analysis comprised 33 619 individuals who worked for at least three years prior to 31 December 1984 at either of two study plants (ie, Saginaw Gear & Axle, Hamtramak, Michigan, manufacturer of rear axle boxes, or Hydra-Matic, Ypsilanti, Michigan, manufacturer of transmissions).

Details regarding data collection have been presented elsewhere (8). Briefly, the following information was abstracted from work records: social security number, year of birth, gender, race, and job history including job titles, departments and dates. Information on vital status through 1984 was obtained from the Social Security Administration and through the National Death Index. Cause of death for those ascertained to be dead was obtained from plant and union records and from state vital statistics offices.

Exposure assessment

A detailed description of the exposure assessment process has been presented elsewhere (16). A review of plant purchasing and industrial hygiene records and interviews with plant personnel provided the basis for assigning type of machining fluid, if any, to each plant-department-job combination in the cohort. Because the types of machining fluids being used changed over time as operations changed, there was a calendar-year dimension to the exposure matrix as well. These assignments were linked with employment records to determine dates of exposure to each fluid type for each study subject. Only jobs held for at least two weeks were abstracted from the work records. Thus, to be included among the subjects considered ever exposed to a particular agent, a worker had to have had a minimum of two weeks' employment in an exposed job.

Analytic methods

Standardized mortality analysis. The USDR (United States death rates) computer package (17) was used to estimate the standardized mortality ratio (SMR) values for cohort subgroups defined on the basis of exposure to the three machining-fluid types. The United States population was used as the external reference population for the estimation of the expected number of cause-specific deaths. A method suggested by David Byar of the National Cancer Institute was used to compute the 95% confidence intervals (17). Because employees were required to have worked at least three years to be included in the cohort, follow-up began at the start of exposure to the agent of interest or three years after the date of hire, whichever was later. The earliest start of follow-up was 1941, as this was the first year in which Social Security Administration records provided complete vital status information. The end of follow-up was 1984 for those known to be alive at the end of the study period, year of death for those who were known to have died during the study period, and last year known to be alive for those lost to follow-up. Because the majority of the employees at the two plants was white, person-time of unknown race was included with white person-time. Person-time associated with missing work history data was considered unexposed.

Poisson regression analysis. The EGRET (epidemiologic graphics, estimation and testing) software package (18) was used to evaluate the association between each of the three types of machining fluid and each cause of death of interest. We developed data sets for each type of exposure for the Poisson regression using a modification of the program suggested by Pearce & Checkoway (19). The data sets contained the number of person-years and number of deaths due to each cause of interest for every combination of covariates. The exposure variables were years of exposure to the agent in question. Categories for each of the exposure variables were formed on the basis of quintiles of the distribution of deaths from all causes. The nonexposure covariates were the following: plant (I, II), gender (male, female), race (black, white and other, unknown), age at risk (five-year groupings from age 20 years through 99 years), year at risk (decade groupings, from 1940 through 1985), length of follow-up (in decades). Study subjects contributed person-time starting three years after hire or 1941, whichever was later. In the internal analysis, we did not want to consider time associated with missing work histories to entail zero exposure, as this is an extreme assumption. Instead, person-time for which exposure data were missing was assigned the average exposure incurred by those working during the missing time interval.

Poisson models were fitted predicting each disease of interest as a function of exposure to one of the three

machining-fluid types, adjusted for plant, gender, race, age at risk, year at risk, and length of follow-up (included as factored terms). The length of follow-up term was included to achieve partial adjustment for the healthy worker effect. For each model, exposure categories were collapsed to achieve a minimum of five deaths due to the cause of interest per stratum. To test for trends in risk with duration of employment, the following approach was taken. The mean duration of exposure for the person-time in each exposure category was used as the value of a new exposure variable, which was included as an unfactored term in models with the same covariates. The P-value associated with the slope for the unfactored exposure variable provided a test of significance of the observed trend.

Results

Vital status was unknown for 6% (N=2201) of the study subjects. Twenty-seven percent (N=9349) of the cohort was known to be dead at the end of the study period. Of these, cause of death was known for 92%. The gender-race distribution of the cohort is presented in table 1. There were 8116 deaths among the white men, 1023 deaths among the black men, and only 258 deaths among the women of either race; thus, the black and white males were the only race-gender groups with sufficient numbers of deaths to bear separate SMR analysis. All of the race-gender groups were included, however, in the Poisson analysis. The SMR results are presented for the white males in table 2 and in table 3 for the black males. The specific causes of death were selected because they were of a priori interest or because they showed relatively stable excesses in at least one of the exposure groups. Results of the Poisson analyses are provided in tables 4 through 6, one table for each type of exposure (straight, soluble, and synthetic machining fluid).

There was some inconsistency between the SMR and Poisson analyses in the ever/never-exposed distribution of deaths because of the different treatment of missing work history data in the two types of analysis (as described in the Methods section). In the SMR analyses, a death would have been included among the ever-exposed only if it was known that the subject was exposed to the agent in question. In the Poisson analyses, in contrast, the person-time for which work history was missing was assigned the average (ie, nonzero) exposure incurred by the cohort in that time period. Thus a death occurring for a subject who had no known exposure but who had an incomplete work history would have been assigned to a nonzero exposure category.

We now summarize the results for each of the selected causes of death.

All causes

For each of the three exposure groups, the all-cause SMR value for the white males was 1.0. For the black males, the SMR values were between 0.8 and 0.9. The Poisson analysis yielded null results for each of the three types of exposure.

Esophageal cancer

The SMR values for the white males suggested a slight excess of esophageal cancer among those exposed to straight oils. There was no excess among the black males. In the Poisson modeling, a general elevation

Table 1. Gender and race distribution of the subjects.

Gender	Race		
	White	Black	Unknown
Male	17 743	5641	6990
Female	1 616	984	645

Table 2. Exposure-specific standardized mortality ratios for selected causes of death by type of machining-fluid exposure among the white males. (SMR = standardized mortality ratio, 95% CI = 95% confidence interval)

Cause of death	Ever exposed to straight oils (N = 13 967)			Ever exposed to soluble oils (N = 23 488)			Ever exposed to synthetic fluids (N = 8446)		
	Number of deaths	SMR	95% CI	Number of deaths	SMR	95% CI	Number of deaths	SMR	95% CI
All causes	3952	1.02	0.98—1.04	7287	1.00	0.98—1.03	1632	1.01	0.96—1.06
All cancer	797	1.01	0.94—1.09	1479	1.02	0.97—1.07	333	0.97	0.87—1.08
Esophagus	22	1.18	0.74—1.79	35	1.03	0.72—1.43	8	0.99	0.43—1.94
Stomach	49	1.12	0.83—1.48	99	1.19	0.97—1.45	21	1.28	0.79—1.96
Colon	59	0.79	0.61—1.03	116	0.85	0.70—1.02	26	0.83	0.54—1.22
Rectum	37	1.47	1.04—2.03	51	1.09	0.81—1.43	9	0.92	0.42—1.74
Pancreas	34	0.80	0.55—1.11	61	0.77	0.59—1.00	19	1.03	0.62—1.61
Larynx	23	1.98	1.26—2.98	30	1.41	0.95—2.01	8	1.57	0.68—3.09
Lung	251	1.02	0.90—1.15	478	1.07	0.97—1.17	116	1.01	0.83—1.21
Prostate	72	1.16	0.91—1.46	125	1.08	0.90—1.28	26	1.11	0.73—1.63
Brain	22	1.08	0.68—1.64	46	1.24	0.91—1.66	6	0.61	0.22—1.33
Leukemia	38	1.25	0.88—1.71	75	1.33	1.05—1.67	16	1.22	0.70—1.98
Cirrhosis	98	1.19	0.97—1.45	173	1.16	0.99—1.35	41	1.04	0.75—1.41

Table 3. Exposure-specific standardized mortality ratios for selected causes of death by type of machining-fluid exposure among the black males.^a (SMR = standardized mortality ratio, 95% CI = 95% confidence interval)

Cause of death	Ever exposed to straight oils (N = 2505)			Ever exposed to soluble oils (N = 4964)		
	Number of deaths	SMR	95% CI	Number of deaths	SMR	95% CI
All causes	457	0.82	0.74—0.90	922	0.81	0.76—0.87
All cancer	100	0.92	0.75—1.12	200	0.90	0.78—1.03
Esophagus	5	0.76	0.24—1.77	10	0.72	0.34—1.32
Stomach	9	1.05	0.48—1.99	17	1.01	0.59—1.62
Colon	3	0.42	0.08—1.23	8	0.55	0.24—1.09
Rectum	1	0.45	0.01—2.53	3	0.68	0.14—1.99
Pancreas	8	1.40	0.60—2.77	19	1.62	0.98—2.54
Larynx	1	0.50	0.01—2.78	6	1.46	0.53—3.19
Lung	35	1.06	0.74—1.48	64	0.91	0.70—1.17
Prostate	12	0.98	0.51—1.72	23	0.98	0.62—1.47
Brain	—	—	—	2	0.77	0.09—2.78
Leukemia	2	0.77	0.09—2.78	4	0.74	0.20—1.90
Cirrhosis	7	0.55	0.22—1.13	21	0.74	0.46—1.13

^a The results for the black males ever exposed to synthetic fluids were not included due to the occurrence of only 30 deaths in this group.

in risk was apparent in association with straight-oil exposure, but a clear dose-response trend was not evident. A similar pattern was observed in the Poisson models of synthetic exposure.

Stomach cancer

In the standardized mortality analysis of white males, stomach cancer was slightly elevated in each of the three exposure groups. Black males showed no excesses. Poisson modeling did not suggest strong dose-response patterns for any type of machining fluid, although in the case of soluble machining fluid there was a very mild elevation in the highest exposure group relative to each of the other strata.

Colon cancer

There was no indication of excess colon cancer in any of the SMR analyses. The results of the Poisson regression were also negative, with the exception of a slight, nonsignificant trend (P -value for trend = 0.16) in risk with exposure to synthetic machining fluid.

Rectal cancer

An excess of rectal cancer was apparent among the white males exposed to straight machining fluid, with a statistically significant SMR of 1.5 [95% confidence interval (95% CI) 1.0—2.0]. There were too few deaths from rectal cancer among the black males to assess associations with types of machining fluid. In the Poisson regression analysis, a trend for rectal cancer risk in relation to years of exposure to straight oils was observed (P -value for trend < 0.001). The rate ratio for the most exposed group (≥ 7.5 years) was 3.2 (95% CI 1.6—6.2). The positive trend with straight-oil exposure was evident at each plant separately, with statistically significant elevations in risk in the highest exposure group.

Pancreatic cancer

While the white males showed no excesses of pancreatic cancer, black males exposed to soluble oils had a statistically significantly elevated SMR of 1.6 (95% CI 1.0—2.5). The Poisson models indicated an unstable elevation in risk in the highest exposure group for synthetic machining fluid.

Laryngeal cancer

Among the white males, the SMR value for laryngeal cancer was elevated in each of the exposure groups, but to the greatest degree in the group exposed to straight machining fluid, with a statistically significant SMR of 2.0 (95% CI 1.3—3.0). There were too few laryngeal cancer deaths among the black males exposed to straight machining fluid to evaluate this association, but the black males exposed to soluble machining fluid exhibited an unstable excess. Poisson modeling provided modest evidence of an association of laryngeal cancer risk with straight-oil exposure, the rate ratio for ≥ 7.5 years of exposure being 2.0 (95% CI 0.9—4.8). The positive association with straight-oil exposure was apparent at each plant.

Lung cancer

The SMR for lung cancer among the white males exposed to soluble machining fluid was slightly elevated, whereas no excesses were observed among the black males. None of the Poisson analyses provided evidence for a positive association of lung cancer with any of the machining-fluid types; a negative association was evident in the case of synthetic (P -value for negative trend = 0.006) and soluble (P -value for negative trend = 0.09) fluids. The negative association with synthetic and soluble oils was evident at each plant.

Table 4. Results of the Poisson regression analysis modeling risk associated with straight-oil exposure for selected causes of death, adjusted for plant, gender, race, time since hire, year of birth, and age at risk. (95% CI = 95% confidence interval)

Cause of death	Exposure to straight oil (years)	Number of deaths due to cause of death	Rate ratio	95% CI
All causes	—	3681	1.0	—
	>0—0.99	1260	1.02	0.95—1.08
	1.00—2.49	1066	1.09	1.01—1.16
	2.50—7.49	1307	1.06	0.99—1.13
	≥ 7.50	1477	0.99	0.93—1.05
Esophageal cancer	—	18	1.0	—
	>0—0.99	8	1.36	0.59—3.13
	1.00—2.49	9	2.06	0.92—4.62
	2.50—7.49	10	1.90	0.86—4.17
	≥ 7.50	8	1.27	0.54—3.00
Stomach cancer	—	50	1.0	—
	>0—0.99	30	1.94	1.23—3.07
	1.00—2.49	8	0.56	0.26—1.18
	2.50—7.49	11	0.63	0.33—1.23
	≥ 7.50	25	1.19	0.73—1.97
Colon cancer	—	59	1.0	—
	>0—0.99	22	1.11	0.68—1.82
	1.00—2.49	21	1.29	0.78—2.13
	2.50—7.49	14	0.76	0.42—1.37
	≥ 7.50	24	0.92	0.56—1.51
Rectal cancer	—	16	1.0	—
	>0—0.99	5	0.93	0.34—2.56
	1.00—2.49	6	1.20	0.47—3.08
	2.50—7.49	9	1.64	0.72—3.76
	≥ 7.50	21	3.17	1.62—6.24
Pancreatic cancer	—	41	1.0	—
	>0—0.99	11	0.78	0.40—1.53
	1.00—2.49	12	1.19	0.62—2.27
	2.50—7.49	12	0.90	0.47—1.73
	≥ 7.50	15	0.87	0.47—1.61
Laryngeal cancer	—	13	1.0	—
	>0—0.99	6	1.26	0.48—3.32
	1.00—2.49	8	1.02	0.41—2.49
	≥ 7.50	11	2.02	0.86—4.75
Lung cancer	—	284	1.0	—
	>0—0.99	79	0.78	0.61—1.00
	1.00—2.49	65	0.94	0.72—1.23
	2.50—7.49	96	1.05	0.83—1.34
	≥ 7.50	91	0.76	0.59—0.97
Prostatic cancer	—	64	1.0	—
	>0—0.99	16	0.83	0.48—1.43
	1.00—2.49	21	1.27	0.77—2.09
	2.50—7.49	24	1.26	0.78—2.03
	≥ 7.50	40	1.52	1.01—2.29
Brain cancer	—	25	1.0	—
	>0—0.99	10	1.12	0.54—2.35
	1.00—2.49	7	1.06	0.46—2.47
	≥ 2.50	10	0.62	0.29—1.32
Leukemia	—	38	1.0	—
	>0—0.99	14	1.11	0.60—2.06
	1.00—2.49	9	0.89	0.43—1.86
	2.50—7.49	14	1.24	0.66—2.32
	≥ 7.50	15	1.08	0.58—1.99
Cirrhosis	—	90	1.0	—
	>0—0.99	37	1.18	0.80—1.73
	1.00—2.49	27	1.24	0.81—1.92
	2.50—7.49	27	0.97	0.62—1.51
	≥ 7.50	33	1.09	0.72—1.65

Prostate cancer

Among the white males but not the black males, the SMR values for prostate cancer were slightly elevated for each exposure group. In the Poisson analyses, there was a mild dose-response trend between prostate cancer risk and exposure to straight machining fluid (P-value for trend=0.03), and the rate ratio for

≥ 7.5 years of exposure was 1.5 and statistically significant. A positive association with straight-oil exposure was apparent at each plant. In the case of synthetic machining fluid, elevated rate ratios were observed, but a monotonic dose-response trend was not evident. In the Poisson analyses there was no association between prostatic cancer risk and exposure to soluble machining fluid.

Table 5. Results of the Poisson regression analysis modeling risk associated with soluble-oil exposure for selected causes of death, adjusted for plant, gender, race, length of follow-up, year of birth, and age at risk. (95% CI = confidence interval)

Cause of death	Exposure to soluble oil (years)	Number of deaths due to cause of death	Rate ratio	95% CI
All causes	—	551	1.0	.
	>0—3.99	1822	0.97	0.88—1.07
	4.00—9.99	2405	1.01	0.92—1.11
	10.0—19.9	2298	0.97	0.88—1.06
	≥20.0	1715	0.88	0.80—0.97
Esophageal cancer	0—3.99	12	1.0	.
	4.00—9.99	15	1.37	0.64—2.95
	10.0—19.9	17	1.57	0.73—3.35
	≥20.0	9	0.96	0.39—2.36
Stomach cancer	0—3.99	29	1.0	.
	4.00—9.99	33	1.06	0.64—1.75
	10.0—19.9	34	1.02	0.61—1.70
	≥20.0	28	1.20	0.69—2.10
Colon cancer	—	8	1.0	.
	>0—3.99	26	1.00	0.45—2.21
	4.00—9.99	36	1.05	0.49—2.26
	10.0—19.9	38	0.99	0.46—2.12
Rectal cancer	—	32	0.86	0.39—1.88
	0—3.99	12	1.0	.
	4.00—9.99	14	1.02	0.47—2.22
	10.0—19.9	17	1.12	0.52—2.40
Pancreatic cancer	—	14	1.15	0.51—2.57
	0—3.99	5	1.0	.
	>0—3.99	21	1.17	0.44—3.11
	4.00—9.99	19	0.88	0.33—2.37
Laryngeal cancer	—	21	0.96	0.36—2.55
	0—3.99	25	1.40	0.53—3.72
	4.00—9.99	12	1.0	.
	10.0—19.9	13	1.64	0.70—3.82
Lung cancer	—	6	0.67	0.25—1.83
	0—3.99	52	1.17	0.38—3.60
	>0—3.99	136	1.0	.
	4.00—2.49	147	0.75	0.54—1.03
Prostatic cancer	—	115	0.71	0.52—0.98
	0—3.99	165	0.82	0.60—1.12
	4.00—9.99	115	0.63	0.45—0.87
	10.0—19.9	11	1.0	.
Brain cancer	—	20	0.54	0.26—1.13
	0—3.99	44	0.86	0.44—1.67
	4.00—9.99	36	0.62	0.31—1.22
	10.0—19.9	54	0.95	0.49—1.83
Leukemia	—	17	1.0	.
	0—3.99	14	0.90	0.44—1.83
	4.00—9.99	13	0.92	0.43—1.96
	10.0—19.9	8	0.84	0.35—2.04
Cirrhosis	—	6	1.0	.
	0—3.99	16	0.77	0.30—1.98
	4.00—9.99	26	0.98	0.40—2.39
	10.0—19.9	19	0.71	0.28—1.80
	—	23	0.92	0.37—2.30
	0—3.99	7	1.0	.
	>0—3.99	58	2.36	1.08—5.18
	4.00—9.99	64	2.35	1.08—5.13
	—	51	2.10	0.95—4.66
	10.0—19.9	34	1.85	0.81—4.21

Brain cancer

There was a slight excess of brain cancer among the white males exposed to soluble oils, the SMR being 1.2 (95% CI 0.9—1.7). There were too few deaths from brain cancer among the black males for the associations with machining-fluid types to be assessed. The Poisson regression did not yield a suggestion of dose-response trends for any fluid type.

Leukemia

Among the white males, leukemia was somewhat elevated in each of the exposure groups; the SMR in the group exposed to soluble oils was 1.3 and statistically significant. Leukemia was too rare an outcome to be investigated among the black males. The Poisson models did not suggest associations of leukemia with any of the machining-fluid types.

Table 6. Results of the Poisson regression analysis modeling risk associated with synthetic-fluid exposure for selected causes of death, adjusted for plant, gender, race, length of follow-up, year of birth, and age at risk. (95% CI = 95% confidence interval)

Cause of death	Exposure to synthetic fluids (years)	Number of deaths due to cause of death	Rate ratio	95% CI
All causes	—	6031	1.0	.
	>0—0.49	1266	1.00	0.94—1.07
	0.50—2.99	601	1.07	0.98—1.17
	3.00—7.99	464	0.97	0.87—1.07
	≥8.00	429	0.89	0.80—0.99
Esophageal cancer	—	32	1.0	.
	>0—0.49	13	2.22	1.14—4.32
	≥0.50	8	1.41	0.57—3.50
Stomach cancer	—	87	1.0	.
	>0—0.49	18	0.95	0.57—1.59
	0.50—2.99	9	1.25	0.60—2.59
	≥3.00	10	0.79	0.38—1.65
Colon cancer	—	93	1.0	.
	>0—0.49	22	1.01	0.63—1.61
	0.50—2.99	6	0.86	0.36—2.02
	3.00—7.99	8	1.41	0.65—3.07
	≥8.00	11	1.61	0.77—3.36
Rectal cancer	—	40	1.0	.
	>0—0.49	9	0.89	0.43—1.84
	≥0.50	8	0.88	0.37—2.07
Pancreatic cancer	—	62	1.0	.
	>0—0.49	12	1.04	0.55—1.95
	0.50—7.99	8	0.91	0.41—2.04
	≥8.00	9	2.04	0.88—4.72
Laryngeal cancer	—	27	1.0	.
	>0—2.99	5	0.89	0.36—2.24
	≥3.00	6	0.63	0.23—1.77
Lung cancer	—	445	1.0	.
	>0—0.49	65	0.76	0.59—0.99
	0.50—2.99	44	0.91	0.66—1.27
	3.00—7.99	31	0.75	0.51—1.10
	≥8.00	30	0.57	0.38—0.84
Prostatic cancer	—	111	1.0	.
	>0—0.49	32	1.32	0.88—1.97
	0.50—2.99	8	1.23	0.58—2.60
	3.00—7.99	6	1.14	0.48—2.71
	≥8.00	8	1.55	0.69—3.47
Brain cancer	—	37	1.0	.
	>0—0.49	11	1.47	0.74—2.92
	≥0.50	4	0.39	0.13—1.20
Leukemia	—	60	1.0	.
	>0—0.49	17	1.25	0.72—2.15
	0.50—2.99	5	1.14	0.44—2.96
	≥3.00	8	1.21	0.52—2.78
Cirrhosis	—	151	1.0	.
	>0—0.49	28	1.03	0.68—1.55
	0.50—2.99	16	1.05	0.61—1.82
	3.00—7.99	9	0.72	0.36—1.47
	≥8.00	10	0.79	0.40—1.59

Cirrhosis

SMR values of 1.2 and borderline significance were obtained in the analyses of white males exposed to soluble and straight oils. No excesses were observed among the black males. No dose-response trend was apparent with any of the machining-fluid types in the Poisson models. There was, however, a twofold excess at each of the exposed levels relative to the unexposed in the case of exposure to soluble machining fluid, on the basis of a small reference group.

Discussion

Overall, our analyses suggested associations of exposure to straight oil with rectal, laryngeal, and prostatic cancers. For each of these cancers, the SMR for those ever exposed to straight oils was elevated, there was some indication in the Poisson modeling of a trend in risk with increasing duration of exposure, and the association was consistent across plants. Suspect carcinogens in straight oils include polyaromatic hydrocarbons (10), long-chain aliphatics (9), sulfur additives (13), and various metals (15) introduced during use.

The use of the two complementary analytic approaches provides a firmer basis for drawing inferences than would the reliance on one of these approaches alone. The external analysis using SMR values suggested a number of possible associations, the credibility of which was supported or disputed by the internal analysis of dose-response trends. The principal strengths of the standardized mortality analysis are the stability of the relative risk estimates and the perspective provided regarding whether mortality patterns in the study population are "unusual." The major weakness of a standardized mortality analysis is the assumption that under the null the death rates in the study population equal those of the reference population (the United States). This concern was addressed in large part by the internal analysis in which the reference group was part of the study cohort, minimizing the likelihood of confounding by nonoccupational factors.

Misclassification of exposure is a major source of concern whenever historical exposures are reconstructed. Despite the comprehensive exposure assessment that was performed for this study, nondifferential exposure misclassification remains likely. This type of misclassification generally biases both the SMR and the Poisson analyses toward the null. In addition, both types of analyses assessed exposures singly. Thus confounding by other types of machining-fluid exposure was possible. However, confounding by concurrent exposures was not likely in the present data, according to the following rationale. None of the three machining-fluid types was negatively correlated with another machining-fluid type, and none of the machining-fluid types is likely to be protective against any cause of death (with the possible exception of lung cancer). Thus only artificial inflation of an association with one machining-fluid type by another machining-fluid type was likely, and for no cause of death did we observe overall associations with two types of machining fluid.

In comparing the results of the standardized mortality analysis with the Poisson regression analysis, one should keep in mind that, while the SMR values have been presented separately for the demographic groups, the Poisson analyses included all of the subjects with adjustment for gender and race. Thus heterogeneity in the SMR values among the demographic groups would not be apparent in the Poisson analyses due to the averaging of rate ratios. Such heterogeneity could reflect random noise or qualitative differences in exposures experienced by the demographic groups.

Our finding of an association of rectal cancer with straight-oil exposure is consistent with the results of a study by Decoufle (2). In his investigation of workers exposed primarily to straight and soluble machining fluids, he reported a slight excess of rectal cancer. Park et al (6) found a statistically significant threefold excess of rectal cancer in a proportionate mortality study of bearing plant workers exposed to machining fluid, but an association with specific fluid types was not ob-

served. Similarly, Vena et al (5) reported a statistically significant threefold excess among workers employed more than 20 years in an engine plant, but the investigators lacked information on personal exposures to specific machining-fluid types.

The suggestion in our data of an association of laryngeal cancer with straight-oil exposure is consistent with reports by Waldron (1) and Ahrens et al (20). In his study of second cancers among men with scrotal cancer, Waldron observed a statistically significant association between laryngeal cancer and work in jobs entailing exposure to straight and soluble oils. In a recent case-referent study, exposure to mineral oils was found to be a risk factor for laryngeal cancer (20). Previous cohort studies have had limited power to detect a modest excess of laryngeal cancer, a relatively rare outcome. Our finding of an association between laryngeal cancer and straight-oil exposure has received further support from an ongoing case-referent study we have undertaken in which the case group has been tripled in size by the addition of incident cases ascertained through registries (21).

Regarding our finding of an association of prostate cancer with straight-oil exposure, the literature provides some evidence of an association between machining-fluid exposure and prostate cancer (22, 23), but it does not provide information regarding specific types of exposure.

Both our SMR and Poisson analyses weakly suggested an association between esophageal cancer and exposure to straight oil. This finding is consistent with a report of a statistically significant proportionate mortality ratio for esophageal cancer in a population exposed to machining fluid (7). This report did not indicate whether the association was specific to straight oils.

The Poisson regression (but not the SMR analysis) provided limited evidence of an association between pancreatic cancer and exposure to synthetic fluids. In contrast, a statistically significant association between straight-oil exposure and pancreatic cancer was previously reported by Silverstein et al (7). Two additional studies have reported associations between pancreatic cancer and machining-fluid exposure, without providing information on specific types of machining fluid (5, 24).

Our observations regarding soluble-oil exposure and cirrhosis, while not providing strong support for an association, are not inconsistent with several previous reports. Silverstein et al (7) noted excess cirrhosis among grinders exposed to oil- and water-based machining fluids at a ball bearing plant. In another study of bearing plant workers (6), a large excess of deaths attributed to alcoholism was observed, and the authors suggested that there may have been misclassification of nonalcohol-related cirrhosis as alcoholism. In the present study, SMR values for oropharyngeal cancers

and accidents, causes of death related to alcoholism, were not elevated in any of the exposure subgroups.

Regarding leukemia, the general elevation of SMR values for each of the exposure groups and the lack of corroboration by the Poisson analysis may be a result of chance, exposure misclassification, or the presence of a nonmachining-fluid leukemogen at the worksite. Similar explanations may apply to our finding of a modest excess of brain cancer in the standardized mortality analysis for soluble-exposed white males and the absence of support from the Poisson analysis.

Stomach cancer was of prior interest on the basis of several studies, which, in toto, suggested an association of stomach cancer risk with soluble machining-fluid exposure (2, 3, 6, 7). Our standardized mortality analysis for white males indicated slight excesses of stomach cancer in each of the exposure groups. While not providing strong support for a causal relationship, the results of the Poisson analysis were not inconsistent with a dose-response relationship between soluble machining-fluid exposure and stomach cancer risk.

With respect to colon cancer, also of a priori interest, our finding of no association with straight or soluble machining fluid, on the basis of robust numbers, suggests that, if this cancer is positively associated with these fluids, the relationship is not strong. A weak dose-response trend was observed for synthetic machining fluid, but this assessment was based on less stable numbers.

In the case of lung cancer, interesting negative findings were obtained. A stable inverse dose-response trend was apparent in the analyses of exposure to water-based fluids (soluble and synthetic machining fluids), while there was no association with straight-oil exposure. This is a noteworthy finding because the water-based fluids are subject to high levels of microbial contamination, including endotoxin-producing gram-negative bacteria, and the inhalation of endotoxin has been hypothesized to exert a protective effect against lung cancer. Gram-negative bacteria (*Pseudomonas*) have been reported in machining fluids at concentrations as high as 108 colony-forming units per milliliter of fluid (25), and in the present study endotoxins were detected in samples of fluid taken at the worksites under investigation (unpublished data). Enterline et al (26) have proposed that the consistent deficit of lung cancer among workers exposed to cotton dust may be due to endotoxins, which may inhibit the growth of malignant cells in the lungs by stimulating macrophage activity, by inducing interferon release, by mitogen activity, or by inducing tumor necrosis factor. Our findings of an inverse association between lung cancer risk and exposure to those fluids prone to endotoxin contamination provide support for this hypothesis.

In light of the fact that soluble machining fluids contain all of the agents found in straight machining fluids, along with additional ones, it is noteworthy that we

found no indication of an association between exposure to soluble oils and the diseases found to be associated with straight oils. On the assumption that straight oils are indeed carcinogenic, perhaps the emulsification of the oils alters the availability of the etiologic agent to the target organs. Alternatively, perhaps dilution in an aqueous solution decreases the concentration of the carcinogenic agent, and our study was not sufficiently powerful to detect the consequently lesser risk associated with soluble-oil exposure.

According to the large study reported here, exposure to straight oils appears to be associated with modest risk for several cancers. Straight oils are still in widespread use in manufacturing operations, and thus exposure to this type of fluid may entail a significant public health impact. Future reports will present detailed exposure-response analyses for specific causes of death, making full use of the exposure data we have assembled on aerosol concentration and the composition of machining fluids.

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