MORTALITY AMONG WORKERS EXPOSED TO CUTTING FLUIDS AND ABRASIVES:

BEARING PLANT II

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Cause of death and job histories were obtained for 1,766 of 2,027 hourly workers with at least 5 year's exposure to cutting fluids and abrasives in the manufacture of ball bearings. Statistically significant excesses of stomach cancer existed among white men with experience grinding in cutting fluids and pancreatic cancer among white men with grinding or machining experience. Stomach cancer excess increased with duration of grinding with statistically significant proportional mortality ratios from 3.4 to 4.2 among those with over 10 years' experience. No association was found between stomach cancer and production machining. Excess proportional mortality was noted from liver cirrhosis, statistically significant among white men in grinding with both oil and water based cutting fluids and among skilled trades machinists. Statistically significant associations were found between lung cancer in white men and work in forging, heat treat and related jobs; lymphopoietic cancer in tool and die workers; and stomach cancer among decendents of French Canadian origin. This confirms earlier findings of digestive cancers and a particular association of stomach cancer with grinding work in water based cutting fluids. Potential carcinogenic agents present include nitrosamines, polyaromatic hydrocarbons, abrasive dusts, and chlorinated oils.

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PREFACE

This is the fourth in a series of six mortality reports conducted under the terms of NIOSH contract #210-81-5104.

The original initiative and preliminary work upon which this investigation rests was accomplished by Dr. Michael Marmor, Laboratory of Biostatistics and Epidemiology, Institute of Environmental Medicine, New York University. This study would not have been done without the continued support of UAW Local Union 626, UAW International Representative Larry Sheridan, and Health and Safety Representative Paul Fortier.

Consultation on the application of logistic regression to mortality odds ratio analysis was provided by Dr. William J. Butler, Department of Biostatistics, University of Michigan. We are particularly thankful for the indispensible and considerable clerical and secretarial efforts contributed by Carole Rogers, Margaret Auch, and Pamela Poe.

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MORTALITY AMONG WORKERS EXPOSED TO CUTTING FLUIDS AND ABRASIVES:

BEARING PLANT II

Prepared by: International Union, United Automobile, Aerospace and Agricultural Implement Workers of America (UAW)

NIOSH CONTRACT #210-81-5104

SUMMARY

Standardized proportional mortality analyses and mortality odds ratio studies were carried out by the International Union, United Automobile Workers, for a population exposed to cutting fluids and abrasives in the manufacture of ball bearings. Earlier study of a similar population found a statistically significant association between stomach cancer and grinding with water-based cutting fluids.

Cause of death and job histories were obtained for 1,766 of 2,027 hourly workers with 5 or more years' plant service who died between January 1, 1950 and June 30, 1983. The major findings were statistically significant excesses of stomach cancer among white men with experience grinding in cutting fluids and cancer of the pancreas among white men with grinding or machining experience. The stomach cancer excess increased with duration of grinding; the statistically significant proportional mortality ratios (PMRs) ranged from 3.4 to 4.2 among those with more than 10 years' experience in various grinding groups. The pancreatic cancer PMRs were also greatest in the longer duration groups in grinding and machining (PMR=2.33-3.50 among decedents with 10 or more years in various jobs). Standardized mortality odds ratio (SMOR) analysis revealed a statistically significant association of stomach cancer mortality with cumulative grinding exposures when controlled for age, year of death, and origin of birth (adjusted odds ratio = 2.3 for 25 years' grinding experience, p=.02, by logistic regression). There was no association between stomach cancer and production machining. Pancreatic cancer mortality was statistically significantly associated with both machining and grinding in straight oil cutting fluids (adjusted odds ratio = 9.9 and 3.2 respectively for 25 years' exposure).

Other findings include: excess proportional mortality (PMR) from liver cirrhosis, statistically significant among white men in grinding with both oil- and water-based cutting fluids and among skilled trades machinists; a statistically significant association (SMOR) between lung cancer in white men and work in forging, heat treat and related jobs; statistically significant increased lymphopoietic cancer (PMR) in tool and die workers; and increased stomach cancer proportional mortality among decedents of French Canadian origin (PMR, SMOR).

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Exposures of potential importance in metalworking facilities include cutting fluids, abrasive dusts, anti-rust oils, and oil smoke. This study confirms prior findings of excesses of digestive cancers and the particular association of stomach cancer with grinding work in water-based cutting fluids. Potential carcinogenic agents include nitrosamines, polyaromatic hydrocarbons, abrasive dusts, and chlorinated oils.

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BACKGROUND

The UAW represents thousands of workers in plants where large-scale machining and precision grinding operations occur, such as bearing, engine and transmission plants. Large numbers of these workers share potential exposure to metalworking or cutting fluids and synthetic abrasives. The first NIOSH National Occupational Hazard Survey estimated that 1,229,000 workers are exposed to cutting fluids; 6,109,000 to any type of mineral oil; 2,137,000 to abrasives; and 1,221,000 to grinding wheel dust.[1]

A considerable body of scientific literature, including epidemiologic and experimental animal studies, has pointed to the possibility of digestive and/or respiratory cancer risk associated with exposure to these materials alone or in combination. The UAW recently completed one such epidemiologic study among bearing plant workers;[2] this report examines a second bearing manufacturer.

A major manufacturer has operated two plants in Connecticut since 1920 for the production of ball bearings. This has involved metalworking processes with extensive use of cutting fluids. In 1978, Dr. Michael Marmor of New York University observed that a large proportion of the occupational dermatitis cases reported to the Connecticut State Department of Labor in the 1940s and 1950s were from these bearing plants. For example, in 1943, out of a total of 1,937 occupational disease notifications of all types and causes, 895 were dermatitis cases originating from these 2 plants. Two hundred of these records specifically listed cutting fluids as the etiologic exposures.[3] Dr. Marmor then proposed an epidemiologic study to determine whether such possibly high and prolonged chemical exposures might be associated with high risk for cancer or other chronic diseases, and performed the initial steps of identifying the cohort at risk and collecting cause of death information. Subsequent discussions led to the study reported here as a collaborative effort.

Study Site

The original employer began to manufacture door bells, bicycle coaster brakes, and ball bearings in Bristol, Connecticut, in the late 1800s. In 1920, the company became a division of a larger manufacturing firm and has continued to produce ball bearings in the Bristol area mainly for automotive and aircraft applications. Employment rose from 5,000 in the early 1920s to a wartime peak of 19,000 in the 1940s, when 10,000 persons worked at the main complex in Bristol and 7,000 worked at the nearby Meriden, Connecticut, facility. Two thousand other workers were located at several smaller plants which closed shortly after the war.

The Bristol plant census declined to about 5,000 by the end of the war and continued a slow decrease thereafter. The Meriden plant population fell to 3,000 at the end of the war, dropping further to a low of 2,000 in 1969 when the plant closed and some of the remaining workers were transferred to Bristol. The consolidated operations in Bristol have employed about 3,000

workers for the past 15 years. Since 1950 more than 10,000 hourly workers have had 1 or more years of plant experience at either Meriden or Bristol.

A UAW local union was chartered in 1939 and, since World War II, has represented most hourly workers at the Bristol plant. Meriden workers had belonged to a separate UAW local union until 1969 when they merged with the Bristol workers. At the present time the local union has about 3,000 active members and 3,000 retirees.

The major processes in the manufacture of ball bearings are: forging, machining and grinding of rings; forming, grinding and honing of balls; heat treatment; and assembly. Other activities include stamping, abrasive tumbling, plating (chrome, nickel, copper), gauging, packing, and various maintenance operations.

The predominant cutting fluids used in the Bristol plant since the 1940s have been mineral oils on most machining operations and water-soluble oil emulsions on most grinding jobs. There have been a few exceptions: secondary machining done after the initial heavy machining in oil (for example, single spindle machines with tungsten-carbide tools) sometimes requires water emulsions; race or form grinding sometimes has been done with oil; ball grinding, which does not involve high-speed abrasive wheels, has been done more slowly with oils, water, or stearate soaps. Synthetic cutting fluids, containing ethanolamines and other additives, were used for short periods on special grinding jobs during the 1970s.

Steel used in the ball bearing industry since World War II has typically contained 1-1.5 percent carbon and chromium. Specialty jobs may require small amounts of manganese or molybdenum. Beryllium-copper steels are sometimes used for bearing manufacture but, according to company personnel, have never been used at these facilities.

Abrasive wheels in these plants have typically been made from ceramic bonded aluminum oxide particles. Phenol-formaldehyde resin binders may also have been used. Silicon carbide abrasives have been used less frequently.

The employer has conducted industrial hygiene surveys in the study plants since 1945. It is difficult to assess the degree to which the sampling results are representative because the surveys have been conducted on an irregular basis, generally in response to perceived problems, and have been directed at a small minority of plant operations. In general, the information about these surveys was insufficient to report on the details of sampling or analytic methods. The major survey results are summarized as follows:

1. Oil mist levels associated with machining (screw machines, bar machines, chuckers) were determined on six occasions from 1949 to 1961. Twenty-four area samples were taken with a mean level of 15.7 mg/m^3 (s.d.=12.6). Thirteen breathing zone samples were taken with a mean level of 15.9 mg/m^3 (s.d.=7.1). A single breathing zone sample of 1.8 mg/m^3 was recorded in 1980. These samples were generally identified as "insoluble oil" or "straight oil."

2. Sampling for mist associated with grinding was not apparently done until 1961 when 3 area samples on ball race grinders were taken with a mean level of 12.5 mg/m^3 (s.d.=5.3). Between 1977-1980 a total of 17 breathing zone samples for total particulate associated with grinding with "soluble oil" were taken with a mean level of 2.2 mg/m^3 (s.d.=1.9). Three breathing zone samples for soluble oil mist were taken during this period, with a mean level of 2.2 mg/m^3 (s.d.=0.5).

3. According to company records, a cutting fluid containing triethanolamine, potassium nitrite and wetting agents (trade name "Lusol") was used on unspecified operations in the late 1940s, but it has not been possible to determine the extent or duration of use. Company and local union representatives both report that nitrites were used widely as rust inhibitors in water-soluble grinding fluids from the early 1950s to about 1980. In addition, nitrites together with triethanolamine were used in synthetic fluids for a short period of time on scattered jobs during the 1970s. No sampling for nitrosamines has apparently ever been done. Two samples for airborne triethanolamine associated with grinding were taken in 1980 (results 0.4 mg/m^3 and non-detectable).

4. Fourteen other miscellaneous area samples for oil mist and smoke have been taken since 1978 on cold header, heat treat, and oil quench operations with a mean level of 1.7 mg/m^3 (s.d.=3.5).

5. A series of airborne dust samples from sand blast operations was taken between 1948 and 1951. Sixteen area samples were reported, with a mean of 2.5 million particles per cubic foot (mppcf) (s.d.=1.9). Eleven breathing zone samples were reported with a mean of 5.3 mppcf (s.d.=5.8). The dust was analyzed in 1949 and found to be virtually all of respirable size and to contain 5-20 percent crystalline silica. A total of 6 samples for dust from grinding operations were analyzed in 1951 and 1961 and reported to contain from 0.5 to 3.87 mppcf of material characterized only as "iron," "aluminum oxide" and "abrasives."

6. Miscellaneous samples over the years have verified the presence of chromic acid, nickel, cobalt, diatomaceous earth, asbestos, methyl chloroform, and benz(a)pyrene in the study plants, but the data are inadequate to determine representative exposure levels or the patterns of use.

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METHODS

Design

Standardized proportional mortality analyses were conducted for all deaths between January 1, 1950 and June 30, 1983 from a cohort of hourly employees of a bearing plant in Bristol, Connecticut. The reference population was the U.S. population. (A cohort or standardized mortality analysis (SMR) was not done because age (birth date) and race information was lacking for most of the surviving cohort.) Case-control analyses (crude and standardized mortality odds ratio) were carried out, examining associations between causes of death and work experience. Seniority lists (listing all current employees) were sampled beginning in 1946 at four-year intervals until 1970. Exposure categories were assigned according to the seniority group and job classifications recorded on the seniority lists.

The prior hypotheses examined were as follows:

1. Cancer of the stomach is associated with grinding exposures involving water-based cutting fluids.[2,4,5]

2. Cancer of the lung is associated with forging and heat treating exposures.[2]

3. Cancer of the lung is associated with grinding in water-based cutting fluids.[2,5]

4. Deaths coded as chronic alcoholism or as liver disease on death certificates are associated with grinding exposures.[2]

Study Population: Definition

The study population was defined as follows: all members of UAW Local Union 626 whose year of termination, for whatever reason, from the study plant was 1950 or later, who died between January 1, 1950, and June 30, 1983, and whose duration of employment, when weighted to account for latency, was at least five years.

Some analyses were conducted on an expanded group for which the minimum duration of employment, unweighted, was five years. The weighting procedure, described in detail under Exposure Measures, diminishes the contribution of an interval of employment depending on how soon it occurred prior to death. The purpose of this weighting was to exclude individuals least likely to have been at risk for long latency disease due to employment at the study plant because of brevity or recency of employment.

The study population consisted primarily of workers exclusively from the Bristol plant but also included a smaller number transferring to Bristol

from the Meriden plant when it closed in 1969. The Meriden workers' years of service definition included time worked at either plant.

Duration of service was based on seniority dates (date of hire) and termination dates obtained from the local union records or from seniority lists. Gaps in employment were detected as missing matches to seniority lists. Thus, only gaps of 4 or more years would be assured of detection; 2-year gaps would have 50 percent chance of detection. Gaps in employment were disregarded in calculation of duration of service (but were taken account of in calculating cumulative exposures).

Study Population: Identification

A dues card file has been maintained by the local union for every union member since before the 1950s. They are believed by union officials to be complete only for the period beginning in 1950. The cards are filed as 1) currently active members, 2) former members not known to be deceased, and 3) members known to have died. Records were abstracted according to a written protocol for all active or deceased workers and for all others in employment at any time after January 1, 1950, providing they had worked at least one year from the date of union initiation until termination of employment from the Bristol plant. Because workers joined the union on a date later than their date of hire, many years later for a substantial number, the requirement of at least one year from union initiation to termination excluded workers with several years of employment who terminated within one year of union initiation. The number of long-duration employees who belatedly joined the union and then left employment within one year is believed to be small (e.g., less than 2 percent of the study population). If employment duration was uncertain, the worker's card was abstracted. Figure 1 shows the major steps in constructing the study population.

The union card files generally contained a date of initiation and/or date of hire and date of termination, but for roughly 20 percent at least one of those was missing. When missing dates precluded an estimate of years of service, the estimate was derived subsequently from seniority list sources.

The records of 10,372 workers were abstracted from local union records. An additional 124 candidates for the study population were obtained from a cumulative pension file maintained by the UAW for this employer. The latter, by definition of pension vesting, listed workers with 10 or more years' service. There were 3,596 matches (using social security number and name) between the pension file and the union members from cards, for whom sex, date of retirement, and approximate date of death (if deceased) were obtained. At the time of matching, the pension file was current as of April 1, 1982.

Vital Status Determination

Vital status for the candidate study population was initially established using: 1) the local union records and 2) the pension file for those known by the employer to be deceased (Figure 1). For those not known to be deceased from local union or pension files (n=8,332), a search was conducted of the Social Security Administration's file of known deaths, using a commercial service (Pension Benefit Inc., Tiburon, California). This Social Security file was current through late 1982 and provided the date of death and, in some cases, the state where a death was recorded. This search yielded 301 additional deaths.

Death Certificate Information

All cause of death information was coded by a single NCHS nosologist, giving both underlying and contributing causes of death. Revisions 6, 7 and 8 of the International Classification of Disease, as appropriate for the year of death, were used except for deaths since 1978 which were coded in ICD-8. ICD-6 and -7 codes were translated to ICD-8 using the conversion program associated with Monson's SMR/PMR program.[6] Coding of the death certificate information for data entry was carried out by one person, using a written protocol, and verified by a different person. Besides causes of death, the following were also coded from death certificates: sex, race, age at death, dates of birth and death, and country of birth.

Initially, transcripts of death certificates for 1,400 study population candidates were obtained by locating original death certificates at the Connecticut Department of Health and transcribing them to a form which reproduced the standard cause of death format: Part I, a,b,c, and Part II. Durations of conditions were also recorded. Because there was a possibility of nosological coding error resulting from inappropriately transcribed death certificates, photocopies of death certificates were obtained for two subsets. The first included 95 deaths occurring over the period 1950-1982 with more than one contributing cause of death indicated on the transcribed record, usually including a malignancy and selected for nosological complexity. The second subset consisted of all 305 other cases in the study population where there was more than one cause of death listed on the transcript, provided: 1) there was any digestive or lung cancer or cirrhosis of the liver; or 2) the deaths occurred 1950-1958 (ICD-6 era). Photocopies were also obtained for all 47 deaths for which transcripts were either ambiguous or indicated that death certificates were illegible. Cause of death was coded from the death certificate when available.

Deaths occurring outside of Connecticut were identified from the local union, the pension file, out-of-state codes in the Connecticut death index and, in a small number of cases, the Social Security file search, and were requested from the States of occurrence. Table 1 gives cause of death acquisition in relation to source of vital status.

Job History and Exposure Classification

Seniority lists for the Bristol plant dating from the 1940s have been retained by the local union. The study population was matched to seniority lists beginning in 1946, at approximately four-year intervals, until 1970. Each list gives a seniority group and seniority (hire) date for each worker employed at the time of the seniority list. (Seniority groups define groups of workers, usually with similar work activities, for the purpose of implementing contract-specified procedures concerning layoffs, transfers, promotions, overtime, etc.) Lists from 1962, 1966, and 1970 gave the current job classification as well. Thus, workers employed in the period 1946-1970 in general had as many as seven seniority group assignments identified at four-year intervals; however, workers transferring from the Meriden plant in 1969 in general had a seniority group identified only once in 1970.

Matching to seniority lists was based on last name, initials and seniority date. For workers for whom no seniority date was available from the local union records, a seniority date was assigned if there was a seniority list match which was validated by 1) other employment information such as union initiation date, estimated hire date from the pension file; and 2) the absence of competing matches. Seniority list matches assigned by computer were examined whenever 1) there was a plausible competing match or 2) a match occurred for a date outside the worker's known employment interval. Matches for which a seniority date disagreement exceeded 5 years were excluded unless there was additional evidence of change in a worker's seniority date or of multiple periods of employment.

A set of 50 broad, process-based exposure categories was defined to cover all the major conditions believed to exist in bearing plant environments (Table 2). The possible seniority group assignments were compiled from the seven seniority lists. Three different employer numbering schemes had been used for seniority groups over the period 1946-1970. There were 145 distinct groups in 1946, 87 in 1950-54, and 51 in 1959-70. Each seniority group was then classified by its dominant exposure category (Table 3) based on knowledge from an inspection of the current Bristol plant, from meetings with plant management and three groups of union members and retirees, from subsequent informal inquiries, from industrial hygiene reports over the period 1946 to 1981, and from the distribution of job classification within seniority groups.

In instances where seniority group classification did not adequately distinguish several likely exposure conditions, a worker's job classification was used in addition, to assign an exposure category (for the years 1962, 1966 and 1970 when job classification was available).

Analytical Variables: Exposure Measures

The exposure categories corresponding to the seniority groups in which each worker spent time were specified. The time accumulated in each distinct exposure category was weighted as follows in order to account for presumed latency of disease and death, in relation to time of exposure:

1. Roughly four-year intervals were defined, centered on the creation date of each seniority list;

2. If the start or termination of employment occurred within one of the four-year intervals, the interval length and mid-point were adjusted accordingly;

3. The time accrued for an exposure category identified by a seniority list match was the length of the interval constructed for that seniority list date multiplied by a logistic weighting function whose argument was the time from the mid-point of the exposure interval until death. The function used is as follows:

$$w(t) = (1+e^{A\,(B\,-\,t)})^{-1}$$

where t is the time from interval mid-point until death, in years, A and B are parameters chosen to determine the shape of the weighting function. The logistic function was selected over other similar functions for ease of computation.

For A = 0.4/ year and B = 12.5 years, the resulting function weights exposures at times prior to death as indicated in Table 4. Thus, exposures remotely in the past have a weight of 1.0, while very recent exposures have weights approaching zero. The weight at 12.5 years prior to death is 0.5. The parameters were chosen to produce a weighting function that plausibly corresponds to the risks of long latency disease, due to previous exposure, such as malignancies of the GI tract or lungs. Since latencies for lung cancer, stomach cancer, and other major epithelial malignancies are generally believed to be 15 to 30 years or more, the choices made for A and B are quite conservative.

4. For workers whose date of hire occurred prior to the first seniority list interval, (the four-year interval centered on 1946), the cumulative exposure in each exposure category was increased by a fixed factor computed individually for each worker. The factor was the ratio of the weighted cumulative time accrued while ever employed at this plant to the weighted cumulative time accrued while employed in the period covered by seniority lists. All workers with job history data had a known date of hire. Exposures later than 1972 were defined to be the same as those indicated by the 1970 seniority list and in any case contributed little to a worker's cumulative exposure (since such exposures occurred within 10 years of death).

Using the cumulative exposure measures, analytical exposure variables for SPMR analysis were constructed by combining various exposure categories as follows:

1. Machining, All Cutting Fluids: includes production machining in oil-based, water-based or unknown cutting fluids (job exposures: 3,4,5).

2. Machining in Oil: production machining almost exclusively in oil-based cutting fluid, i.e., straight cutting oil (job exposure: 3).

3. Machining in Water: production machining often in water-based cutting fluid, i.e., soluble oils, synthetics (job exposure: 4).

4. Grinding, Comprehensive: a broad set of exposure categories which include production grinding in oil-, water-based or unknown type of cutting fluid, on both rings and balls (rough grind only), skilled trade grinders (not tool and die or tool grinding), and material handlers and inspectors associated with production grinding (job exposures: 8,11,12,13,14,31).

5. Grinding, Restrictive: includes production grinding in mixed water and oil, water-based or unknown cutting fluids and a skilled trade concentrating on grinding (a subset of Grinding, Comprehensive; job exposures: 11,12,13).

6. Grinding in Water/Oil: production grinding where both oil- and water-based cutting fluids were used (job exposure: 11).

7. Grinding in Water: production grinding predominantly in water-based cutting fluids, and a skilled trade concentrating on grinding (not tool and die) (job exposure: 12).

8. Tool and Die: excluding tool sharpeners (job exposure: 50).

9. Tool Grinders: tool sharpeners (job exposure: 22).

10. Forge, Heat Treat: includes forging, ball heading, heat treating of balls, rings and cutting tools, and annealing (job exposures: 1,2,9,10,36).

11. Skilled Trades Machinists: includes both machining and grinding in non-production jobs (job exposures: 28).

12. Assembly, Packing: includes assembly, packing, shipping, ball inspection, mill supply, and quality control standards checking (job exposures: 23-26,30,35).

For the machining exposure groups, a relatively clear separation was possible between jobs using oil cutting fluids almost exclusively ("machining in oil"), and jobs with some oil use but substantial usage of water-based fluids ("machining in water"). For the grinding exposure groups, this distinction was less clear. Water-based cutting fluid use predominated in "grinding in water" jobs (along with some oil-based fluid use); for the "grinding in water/oil" jobs, there was probably substantial use of both types of cutting fluids; however, these were the jobs with the most use of oil-based fluids. All of these judgments were qualitative and process-based, not based on industrial hygiene sampling. It is likely that actual exposures to water-based cutting fluid mists and splashing is higher in the types of grinding classified as "grinding in

water/oil" (usually race grinding) than in those jobs classified as "grinding in water" (usually surface and outside diameter grinding).

For SPMR analyses, variables were defined indicating whether a worker had accumulated between 40 and 119, or 120 or more months (in weighted time) in these exposure groupings. Table 5 shows the distribution of the study population in those exposure variables.

For case-control studies (crude mortality odds ratios), a set of variables was constructed in which each member of the study population was assigned a status of exposed, unexposed (comparison group) or excluded. In exposed status, for a particular exposure category, cumulative weighted duration as much as 60 or 120 months was variously required (a higher minimum exposure requirement than in the SPMR selections in order to heighten the contrast). For the unexposed (comparison) status, the aggregate cumulative duration in the exposure categories of interest and in other exposures known to be or suspected (a priori) of being associated with the cause of death of interest had to be less than 12 months. Table 6 shows the exposure categories utilized in defining the exposed, unexposed and excluded. Workers with limited job histories — whose known exposure category of longest duration was less than 40 months — were excluded from the unexposed category in case-control analyses because of the possibility that the unknown portion of their job history might include important exposures (either the exposure of interest, or others to be excluded).

Analytical Variables: Outcome Measures

For crude mortality odds ratio analyses, outcome variables were defined in which "cases" were those deaths due to particular underlying causes, and "controls" were all other deaths with the exception of 1) causes excluded from analysis because they too were suspected or known (a priori) to be associated with the exposure being investigated, and 2) all deaths for which the outcome of interest was a contributing but not underlying cause of death. Table 7 shows the major outcome variables and their exclusions.

Analysis

Standardized proportional mortality analysis was performed using Monson's program and reference rates for the U.S. national population, updated through 1980.[6] Analyses were performed for major subpopulations based on exposure and origin of birth. Two-tailed P-values and confidence intervals were computed using the Mantel-Haenszel chi-squared statistic generated by the PMR program for causes of death where the expected number of deaths was five or more; for all others, a two-tailed Poisson P-value and intervals were computed.

Crude mortality odds ratio analyses[7] were performed for selected associations (based on PMR results or prior hypotheses), using the exposure and outcome variables already described. Crude odds ratios were computed

and statistical significance determined using the Fisher Exact test. Age at death, year of death and origin of birth were examined for association with exposures and possible confounding. Live controls from the cohort were not used, in part, because age, race and location of birth were available only for decedents. The use of social security numbers to infer date of birth[8] was inappropriate for this population because large numbers of employees had been assigned consecutive social security numbers by government agents going through the plant department by department in the late 1930s or early 1940s. Another reason for using dead controls was to make cases and controls more comparable on nonwork-related risk factors, such as smoking. The use of the latency requirement in defining the study population insured that short-term employees with high mortality would be excluded.

Because important confounding was potentially present, standardized mortality odds ratios (SMOR) were calculated for the key associations, using logistic regression, simultaneously adjusting for age at death, year of death and origin of birth, while estimating concurrent exposure effects.[9] (See Appendix for a more detailed description of this method.) The algorithm used computes an unconditional, maximum likelihood estimate, and is contained in the BMDP(3R) statistical program.[10] The outcome measure (case/control) for SMOR analyses involved no exclusions — controls were all non-cases — for computational simplicity. The logistic regression modeled the odds of being a case — i.e., of a death having resulted from a specified underlying cause. Adjustment for age at death and year of death in the logistic regression analyses was performed utilizing proportional mortality rates for the U.S. national population. The expected odds of having died from a particular cause, specific for age, year of death, race and sex was computed, and the log (odds) was included as a term in the logistic regression model with a coefficiant fixed at 1.0. Other terms included were indicators of origin of birth and cumulative durations (weighted) in specific exposure categories (with no exclusions or minimum durations required). The general model used was as follows:

$$\ln\left(\frac{p}{1-p}\right) = a_o + 1.00 \ln\left(\frac{r_i}{1-r_i}\right) + b_1 I_B + \ldots c_1 X_1 + c_2 X_2 + \ldots$$

where r_i is the age-, year-, sex-, race-specific proportional mortality rate for the cause of death of interest, in U.S. population;

I_B is origin of birth indicator;

X_i is cumulative exposure in category i;

a_o, b_i, c_i are coefficients to be estimated.

Models were fitted for the major associations described from SPMR and crude case-control analyses. Selected birth indicators were tested if there was evidence from the SPMR analyses, apparent association with exposures, or prior knowledge of their importance. The exposures tested were those with associations from SPMR or case-control analysis; of the several exposure variables defined for machining and grinding jobs, one or more were tested

and the strongest contributor to the model was retained. The contribution of each risk factor to the final model was assessed by removing that one variable and computing a P-value for the change in 2log(likelihood), which is approximately distributed as chi-squared, with 1 degree of freedom.[11] For prior hypotheses, a one-tailed P-value was used, otherwise a two-tailed P. Summary statements of estimated odds ratios, from logistic regression, are given as the odds ratio with respect to 25 years' (weighted) duration of exposure.

All analyses, SPMR, case-control, and logistic regression were restricted to white workers, the non-white population being too small for meaningful analysis. Most analyses focused on white men for the same reason.

RESULTS

Study Population Characteristics

Of the 2,597 deaths identified in the candidate study population of 10,496, 2,027 satisfied the study population selection criteria including the minimum duration of work, weighted for latency (see Methods); 516 failed to satisfy the selection criteria, and 54 others were excluded for insufficient information on the selection criteria (Fig. 1). (When weighting was removed from the requirement for a 5-year minimum duration, 186 additional cases for a total of 2,213 were available for analysis.) Approximately 250 deaths in the candidate study population were excluded because the date of death or date of employment termination came prior to 1950.

Cause of death was available for 92 percent of the study population, and for 87.1 percent or 1,766 both a job history and cause of death information were obtained. Table 8 shows the study population by sex and race.

Table 9 gives the white male study population distribution by origin of birth, ages of hire and death, and year of death. U.S.-born constituted 62 percent of white men in the study population, the other major groups being Central European, Canadian (largely from French Canada) and Italian. Deceased workers not born in the U.S. or Canada had been hired at considerably older ages than the others. Age at death was generally higher in the non-U.S. population; more than half of deaths in those born in Europe occurred past age 75. Year of death for the non-U.S. born group tended to be earlier; 65 percent of Central European deaths but only 40 percent of U.S. deaths occurred prior to 1970.

There were associations between origin of birth and exposure classification. Table 10 gives the white men of the study population in exposures of longest duration and by origin of birth (weighted durations used; see Methods). Forging (and ball heading) had a smaller proportion of workers of Italian descent, while in heat treating such workers were over-represented compared to the study population as a whole. Workers of Central European origin were over-represented in heat treating and machining. Canadian workers were over-represented in grinding and tool grinding. Generally, non-U.S. workers were under-represented in the skilled trades categories (tool and die, machinist, other). Most white women in the study population were in assembly (77.1 percent) or inspection (19.8 percent) jobs.

There is also some association of age at death, year of death and age of hire with exposures of longest duration (Table 11). Deceased workers whose exposure of longest duration was machining or grinding had a higher proportion with age at death below 55 than the rest of the workers.

Validation of Death Certificate Transcriptions

For the transcripts selected for coding difficulty, there were 16 transcript-certificate pairs out of 95 with conflicting ICD codes for underlying cause of death. In seven discordant pairs, both codes were for non-malignant disease. (Table 12) In seven other discordant pairs both had codes for malignancies. Two of these pairs involved stomach cancer. One involved brain cancer and none involved pancreatic cancer. In three, the code from the transcribed source was malignant neoplasm without specification of site.

Obtaining death certificates for all other transcripts in which coding of underlying cause would involve digestive or lung cancer, or cirrhosis of the liver (and all ICD-6 multiple cause deaths), produced only 20 3-digit discordant pairs out of 305. None involved cancers of the stomach, pancreas or lung. Three cases with colon cancer coded from transcript were coded as rectal, unspecified cancer and heart disease from certificate. There were two cases where cirrhosis of the liver was coded for deaths previously coded as heart disease and diabetes. Two cirrhosis cases from transcripts were coded as pneumonia and rupture of urinary bladder due to a fall.

Standardized Proportional Mortality Analyses

SPMRs were calculated for the 1,532 white men with both job history and cause of death. There was a slight elevation in proportional mortality due to all cancer and a larger, highly significant increase due to digestive cancer, concentrated in the stomach (PMR=35/17.7=1.97, $p < .001$), colon (PMR=41/29.6=1.39, p=.04) and pancreas (PMR=24/16.8=1.43, p=.08). (Table 13) Four additional stomach cancers appear if those lacking job histories are included (84 additional white men). All non-malignant digestive disease is also elevated in this population (PMR=76/61.51=1.24, p=.06) largely appearing as cirrhosis of the liver. All circulatory disease is very close to the expected, arteriosclerotic disease is slightly elevated (PMR=1.10, p=.002), and all respiratory disease slightly reduced (PMR=.91). There were three deaths due to skin diseases for one expected, and a substantial deficit of deaths due to accidents and suicide. When the analysis is limited to those with 10 or more years' (weighted) duration of employment, the PMRs for digestive cancer increase slightly (Table 14): stomach cancer PMR=2.08, colon cancer PMR=1.45, and pancreas cancer PMR=1.45.

When the study population specification requiring a minimum weighted duration of employment of five years was modified to become a minimum unweighted duration of employment, the overall PMR analysis was largely unchanged. With 131 additional white men (with job history and cause of death), the PMR for all digestive cancers remained 1.52; for stomach cancer the PMR went from 1.97 to 2.00 and for colon cancer from 1.39 to 1.46. For cancer of the pancreas, the PMR went from 1.43 to 1.38 with the unweighted selection. The lung cancer PMR went from 0.92 to 0.98, and cirrhosis from 1.34 to 1.37 in the larger study population.

Analyses for all white women with both job history and cause of death reveal no elevations in proportional mortality due to digestive diseases, either malignant or non-malignant (Table 15), except for cirrhosis of the liver (PMR=2.26, p=.08). Heart disease, non-malignant respiratory disease and all external causes showed the same pattern as for men. If 22 additional white women lacking job histories are included, the pattern is unchanged except that cirrhosis of the liver is further elevated by 2 new cases.

When the study population is stratified according to origin of birth, several results emerge (Table 16). Men born in the U.S. had less elevated proportional stomach cancer mortality (PMR=1.53, p=.10) and more colon cancer mortality (PMR=1.61, p=.01), while those of Central European birth had more stomach cancer (PMR=6/2.3=2.6), based on small numbers. Men of Canadian origin (largely from French Canada) had a distinctly high proportional mortality due to digestive cancers (PMR=20/9.7=2.06, p=.001), especially stomach cancer (PMR=9/1.96=4.58, p=.001). The pattern for men born in Italy was not distinguishable, given small numbers, except possibly for cancer of the rectum (PMR=3/.74=4.03, p=.08). Among the origin of birth strata, the U.S.-born have a later year of death and the Central European and Italian births have somewhat higher ages at death (Table 16).

SPMR analyses done for white men in major exposure groupings (10 or more years' weighted duration) reveal that the stomach cancer excess was concentrated in Grinding, Comprehensive (see page 11) (PMR=13/3.8=3.39, p .001), and absent in Machining, all cutting fluids (PMR=2/1.89=1.06). (Table 17,18) Pancreatic and colon cancer were elevated in both groups but statistically significant only for Grinding. Non-malignant digestive and respiratory diseases were not statistically significantly elevated in either group. These two exposure groups are not mutually exclusive: 11 workers had more than 10 years' duration in both. These analyses do not adjust for origin of birth differences between exposure groups.

SPMR analyses for the grinding and machining groups, defined using unweighted durations of employment in the corresponding larger study population, produced slightly different estimates for cancer of the stomach and pancreas. For Grinding, Comprehensive (10 or more years duration), the stomach cancer PMR was 3.39 with weighted duration and 2.94 with unweighted, and for cancer of the pancreas, 2.33 weighted and 1.85 unweighted. For Machining, all cutting fluids (and some associated jobs), the cancer of the pancreas PMR was 2.95 for weighted duration and 2.72 for unweighted duration.

Restricting exposure groups to jobs with exposure to specific classes of cutting fluids, and comparing those having 40-119 months exposure with those having 120 or more months (10 years), allows further localization of excess proportional mortality, but without taking origin of birth into account (Tables 19-23 and summarized for digestive diseases in Table 24). In Machining (Table 19), the two-fold increased proportional mortality due to colon cancer cannot be further associated with any subgroup. For the increased pancreatic cancer, with small numbers, the PMR is highest in machining in oil cutting fluids for the longer durations (PMR=4.67, p=.06). For grinding (Tables 20, 21), stomach cancer increases with duration in all the grinding exposure groups. It is greatest for 10 or more years in grinding in water (PMR=4.00, p=.08) and in

water/oil (PMR=4.15, p=.02) cutting fluids. Cancer of the pancreas also increased with duration in each grinding subgroup. The non-malignant digestive diseases were in greatest excess in the grinding in water/oil exposed workers. Colon cancer was elevated across all grinding groups.

There was increased digestive disease proportional mortality in the skilled trades groups — tool grinders, tool and die workers, and machinists — and in forge and heat treat workers, but each of these groups was small (Table 22). Stomach cancer was significantly elevated for tool grinders (PMR=3/.58=5.1, p=.04), and pancreatic cancer was elevated but not significantly for machinists. Liver cancer was elevated in Machining (Table 18) and for machinists and tool and die workers (Table 22), who potentially share common exposures. Taken together, there are 6 observed, 1.24 expected.

PMRs for stroke were generally below 1.0 except for those with 10 or more years in grinding, where there were small excesses. For grinding in water/oil, the stroke PMR was 1.31 but not statistically significant. Similarly, PMRs for all non-malignant respiratory disease were generally less than 1.0 except for those in grinding, the largest being for grinding in water/oil (PMR=10/7.4=1.36, p=.16). (Table 21)

All lymphopoietic cancer was elevated in tool and die and tool grinding workers (with 10 or more years' exposure). A number of workers had substantial durations of exposure in both categories. For workers with 10 or more years in the composite grouping of tool and die and tool grinding, the lymphopoietic cancer excess was highly significant (PMR=9/1.83=4.01, p=.001). There was no similar elevation for skilled machinists, other skilled trades or for the major production groups - machining, grinding, etc.

The Forging, Heat Treat exposure category had an overall excess in cancer proportional mortality (PMR=35/25.=1.39, p=.05), with the elevations concentrated but not statistically significant in cancer of the lung, rectum and esophagus (Table 22). The PMR for lung cancer was 1.34 in this category using unweighted duration, compared with 1.54 using weighted selection (both based on the same 11 cases).

The white male assembly and packing exposure group also experienced some elevated digestive cancer including a statistically significant excess of stomach cancer (PMR=5/1.4=3.5, p=.03), together with increased non-malignant digestive disease (Table 23). Some assembly jobs are in close proximity to grinding operations and some assembly workers had both assembly and grinding experience. For women assembly workers, the only indication of excess digestive disease proportional mortality was an elevated proportion of deaths due to cirrhosis of the liver (PMR=4/1.5=2.59), which was not statistically significant (Table 23, 24).

Case-Control Analysis: Crude Mortality Odds Ratios

Cancer of the Digestive System

Table 25 shows crude mortality odds ratios for stomach cancer unadjusted for origin of birth, age and year of death for some major exposure groups. Stomach cancer was associated with most of the grinding subgroups (which are not mutually exclusive). The odds ratios were consistently higher in the groups with longer duration and were statistically significant in workers with longer durations in Grinding, Comprehensive (odds ratio=2.37, p=.03); Grinding, Restrictive (odds ratio=2.68, p=.04); and grinding in water/oil (odds ratio=3.28; p=.04). In tool grinders the association was not significant (odds ratio=3.67, p=.08). All machining exposures had odds ratios less than one.

For the association of stomach cancer with Grinding, Comprehensive, the age at death distribution is similar for the exposed and comparison groups; the exposed group generally has a later year of death and has double the proportion born in Canada. (Table 26) Similar potential for confounding was found for the other grinding-related exposure groups. For tool grinding, age at death, year of death and origin of birth were roughly comparable between the exposed and comparison groups; those of European descent were under-represented in the exposed group (Table 26).

Case-control results for colon cancer for machining and grinding exposures are given in Table 27. Most of the odds ratios are close to 1.0 and none is statistically significant.

Case-control results for cancer of the pancreas are given in Table 28. In Machining, there was a possible trend with increasing duration and likely exposure, and a statistically significant result for longer duration oil-based cutting fluid exposures (odds ratio=5.31, p=.05). However, the risks for machining in oil and in water-based fluids cannot be distinguished. In grinding, none of the associations is statistically significant, but the odds ratios are consistently greater in the longer duration groups. Furthermore, the comparison group, specified a priori, includes machining exposures, now observed to be associated with pancreatic cancer. Table 29 shows the potential confounders for the cancer of the pancreas associations. Age at death differed somewhat between the grinding exposure and comparison groups but was quite similar for the machining and comparison groups. There were differences between the exposure and comparison groups for year of death and location of birth. Those of Canadian birth were over-represented in both machining and grinding exposures but constituted a small group.

Non-malignant Digestive Disease

Crude odds ratios for non-malignant digestive disease (ICD-8: 520-579; includes GI ulcers, diseases of liver, gall bladder, pancreas) show a statistically significant excess only for grinding in water/oil for more than 10 years. There are no indications of excess digestive disease in machining. When digestive disease was limited to cirrhosis of the liver (Table 30), the odds ratio for the

grinding in water/oil group was 3.3 (p=.04); potential confounders are similarly distributed except that the exposed groups were more likely to have died 1960-1979.

Cancer of the Lung

Case-control analysis for those with employment in forge, heat treat and allied processes for 10 or more years resulted in a statistically insignificant elevation in lung cancer (odds ratio=1.50, p=.17), as in the SPMR analysis. Potential confounders were distributed similarly between the exposed and comparison groups, but the exposed died more often between age 65-74.

Stroke and Non-malignant Respiratory Disease

In comparing deaths for workers with 10 or more years' weighted duration in grinding in water/oil with non-grinders, the crude mortality odds ratio for stroke was 1.86 (p=.05). Other comparisons yielded no associations. For the grinding in water/oil association, age of death, year of death and location of birth were similar in the exposed and comparison groups except that those of Canadian birth were over-represented in grinding (17.7 vs. 8.2 percent).

Also elevated in grinding, but not statistically significant, was non-malignant respiratory disease excluding pneumonia (ICD-8: 491-519; OR=1.6, p=.1). For this comparison, the exposed group was more likely to have died in the years 1970-1983 than the comparison group (59 percent vs. 46 percent), which implies positive confounding because respiratory disease proportional rates are increasing 1950-1980.

Logistic Regression: Standardized Mortality Odds Ratios

Stomach Cancer

In the final model, there was a statistically significant effect of weighted exposure duration in Grinding, Comprehensive (p=.024, one-tailed test, Table 31). The effect estimate, applied to 25 years of weighted exposure, produces a standardized mortality odds ratio (SMOR) of 2.25. The SMOR for stomach cancer in those of Canadian origin was 2.56 (p=.015), and for tool grinding the odds ratio was 3.38 (p=.10, one-tailed test) for 25 years of exposure. The estimated stomach cancer SMOR for the unexposed study population, obtained from the model intercept, was 1.29. Substituting Grinding, Restrictive, in the same model, resulted in a slightly larger and less certain estimate for grinding (odds ratio = 2.30 for 25 years' duration, p=.033) and a smaller estimate for tool grinding (odds ratio =3.05 for 25 years' duration).

When an indicator of birth in Central Europe, a known risk factor, was included in the final model, the resulting effect was sizeable but not statistically significant (OR=1.78, p=.13). The estimate resulting for grinding was slightly

smaller (OR=2.22), and that for tool grinding larger (OR=3.59); the SMOR for the unexposed population (and not of Central European or Canadian birth) was then estimated to be 1.16. Interactions between the Grinding exposure measure and age at death, year of death, or birth in Canada were tested. For the age interaction there was no effect; for year of death there was a weak negative year dependence (suggesting a slightly declining risk for Grinding over time) that was not statistically significant. The exposure-birth in Canada interaction was small, negative, and not significant.

Cancer of the Pancreas

There was no evidence of an origin of birth dependence for cancer of the pancreas in either the SPMR studies or the SMOR analysis. In the final model, large, statistically significant effects were found for both machining and grinding exposures (Table 32). For machining in oil, the 25-year odds ratio was 9.9 (p=.014, two-tailed test), and for Grinding, Comprehensive, it was 3.2 (p=.02). For grinding, the best fit was with an interaction involving date of hire. Including grinding exposure, date of hire (in months since March 1933, the population mean date of hire), and the exposure-date of hire product term resulted in an odds ratio for grinding exposure that was large for early hire dates and fell to below 1.0 for dates of hire after 1935. The odds ratio for 25 years of grinding with date of hire in 1923 was 3.1; for date of hire in 1918, the odds ratio was 4.8. Inclusion of the grinding and interaction terms had a p-value (two-tailed) of .018. There were no age, year of death or year of hire interactions with the machining in oil exposure. The primary machining steps have always been done on lathes in oil in this plant; grinding was traditionally done in oil until soluble oil emulsions were introduced after the 1930s. When machining in all cutting fluids was substituted for machining in oil in the model, the effect-estimate was smaller; the 25-year odds ratio was 4.5 and not quite as statistically significant. The all cutting fluids measure included machining in water or unkown cutting fluids in a variety of jobs in addition to the multi-spindle lathes operating in oil.

Cancer of the Colon

There was excess colon cancer among machining and grinding exposed workers in SPMR but not in case-control analyses. In adjusting for age at death, year of death and origin of birth, no machining exposure association remained by logistic regression analysis. For Grinding, Comprehensive, there was a small statistically insignificant effect (OR=1.7, 25 years' exposure, p=.18, two-tailed test). A large but not significant effect of U.S. birth was estimated (OR=1.61, p=.08, one-tailed). The SMOR estimated for the rest of the study population was 1.01.

Cancer of the Lung

Table 33 shows the logistic regression analysis for cancer of the lung. There was no origin of birth effect. The exposure variable consisting of weighted duration in any of forging, heat treat, ball heading or annealing was

a statistically significant predictor of lung cancer mortality odds. The estimated adjusted odds ratio, for 25 years of exposure, was 1.99 (p=.035, one-tailed test). There were no indications of effect for machining, or tool and die exposures; for Grinding, Comprehensive, there was a negative association that was not statistically significant. There were no age or year of death interactions in the association of forge, heat treat exposures and lung cancer.

Non-Malignant Digestive Disease

Standardized mortality odds ratios were computed for the exposures with excesses in cirrhosis of the liver as seen in SFMR and case-control analyses: grinding in water/oil and for machinists (Table 34). For machinists, using weighted duration of exposure, the 25-year odds ratio was 6.08 (p=.07, two-tailed). Using an indicator for any exposure in excess of five years weighted duration, the odds ratio was 3.13 (p=.12, two-tailed). For grinding in oil, the 25-year odds ratio was 2.7 but not statistically significant (p=.16, two-tailed). It is likely that the weighted duration of exposure measure (used throughout) is less appropriate for non-malignant liver disease than for cancer outcomes.

Goodness of Fit

The appropriateness of the models fit to the data using logistic regression was assessed by defining strata for the continuous cumulative exposure measures, computing the numbers of cases predicted by the model in each stratum and comparing with the observed. This was done for the key models involving stomach, pancreatic and lung cancer (Table 35). Tests of goodness of fit were not done because the number of cases were small and the apparent fit was very good.

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LITERATURE REVIEW

Nature of Machining and Grinding Exposures

Metal products which have been roughly shaped by casting, stamping, and forging processes often require further removal and smoothing of metal to attain precise size and shape specifications. "Machining" refers to processes such as milling, turning and boring in which metal is sliced or cut from a workpiece by the application of a sharp, hard-tipped tool at relatively low speeds and temperatures (less than 1000°F).[12] "Grinding" removes fine particles of metal with abrasive wheels applied to metal surfaces at relatively high speeds, producing temperatures as high as 2000°F. Both machining and grinding generally require the use of cutting fluids directed in a stream or mist to the working surface for lubrication, cooling and the removal of metal debris.

Metalworking cutting fluids belong to three classes:

1. Cutting oils (also called insoluble or straight oils): These may be naphthenic or paraffinic mineral oils with added polar lubricants of animal and vegetable origin such as lard or sperm oil. Chlorine, sulfur or phosphorus based additives are frequently used to improve lubricating properties.

2. Soluble oils (also called water miscible or emulsified oils): These fluids contain emulsifying agents such as petroleum sulfonates or amine soaps to suspend oil droplets in water. Chlorine, sulfur and phosphorus based additives are often used to improve lubrication. Other additives include corrosion inhibitors (e.g. nitrites, polar organic compounds), chemical stabilizers (e.g. complex alcohols and non-ionic wetting agents) and biocides (e.g. triazines).

3. Synthetic fluids (also called chemical fluids): These are generally alkaline water solutions such as ethanolamines with added corrosion inhibitors (e.g. nitrates, nitrites, borates, phosphates), surfactants (e.g. complex alcohols and esters), non-mineral oil lubricants (e.g. silicones), and biocides (e.g. triazines).

Straight cutting oils have been used since the early days of the industrial revolution, whereas soluble oils and synthetic fluids have been used widely only since the 1940s. Straight oils are still used today in many machining and some grinding applications because of their lubricating qualities, while soluble oils and synthetics are particularly useful for grinding because of their cooling properties. There is, however, considerable overlap in usage.

The use of cutting fluids invariably produces an aerosol both mechanically and by vaporization and condensation. Straight oils tend to produce larger and heavier droplets than the finer mists associated with synthetic fluids.[12] The present OSHA standard for oil mist exposure is 5 mg/m^3.[13] This standard was based on animal test data for exposure to straight mineral oils

and was aimed primarily at the prevention of lipoid pneumonia from gross exposures.[14] There is no specific standard for the synthetic fluid mist.

Oil mist measurements in metalworking plants in the past several years have typically been in the 0.5-5 mg/m^3 range. A NIOSH evaluation in an automotive transmission plant using soluble oils reported personal sampling exposures from 0.07 to 1.4 mg/m^3.[15]

Jarvholm reported area samples from a bearing plant similar to the one in this study.[16] Oil mist levels ranged from 0.3-2.3 mg/m^3 in the turning department (machining), 1.0-7.3 mg/m^3 in grinding, and 0.4-18.0 mg/m^3 in hardening (heat treat) with mean levels of 2.0, 3.2, and 2.9, respectively. Decoufle reported personal samples ranging from 0.4 to 1.67 mg/m^3 of mist in an engine plant using predominantly straight mineral and soluble fluids.[5] In this latter study the geometric mean droplet size of mineral oil mist in various samples ranged from 2.4 to 5.6 um. Droplet sizes for aerosols of the soluble and synthetic fluids were not reported but were presumably smaller.

There are four specific groups of toxicologically suspect chemicals associated with these mists in metalworking operations:

1. Polycyclic aromatic hydrocarbons, including benz(a)pyrene, have been measured in both new and used bulk samples of straight oils.[17] Solvent refining of these oils in recent years is thought to have reduced the level of these contaminants below that historically found in acid-refined oils.[17,18] Recent measurements on bulk samples have found 0.5 to 150 pg/ml of benz(a)pyrene in new oils and higher levels in used oils.[19]

2. N-nitroso compounds, including nitrosamines such as N-nitrosodiethanolamine, have been detected in bulk samples of synthetic metalworking fluids. These presumably result from the combination of ethanolamines and nitrite additives in solution. Fan has measured concentrations of N-nitrosodiethanolamine as high as 3 percent in new bulk fluid concentrates.[20] A recent NIOSH survey found considerably lower levels (0.2 to 600 ug/ml) in a variety of new and used fluids.[21] Nitrosamines in fluids diluted for use were generally at the lower end of this scale. Only trace amounts were found in air samples; however, the testing procedures were designed to measure nitrosamine vapors and not mist-borne nitrosamines.

   N-nitrosodiethanolamine is known to be absorbed through human skin[22] and has been measured in the urine of metal grinders.[23]

   In 1976, NIOSH issued a "Current Intelligence Bulletin" to alert cutting fluid manufacturers, users and workers about the potential hazards of these exposures.[24] In January 1984, the U.S. Environmental Protection Agency published a proposed rule which would prohibit the addition of nitrosating agents to the triethanolamine salt of tricarboxylic acid when used in metalworking fluids.[25]

3. Biocides are typically added to all varieties of cutting fluids to reduce microbiologic growth. Those commonly used in water-based fluids have

recently been reviewed and include a wide variety of organic compounds.[26] The most common are cyclic triazines which are condensates of formaldehyde with substituted alkylamines or ammonia. Although it is presumed that these act by releasing formaldehyde under normal conditions in alkaline cutting fluids, very little effort has been made to examine this under field conditions.

4. Abrasives: Grinding wheels have been made predominantly from silicon carbide or aluminum oxide since the 1920s, when these synthetic abrasives were introduced to reduce the silicosis hazard associated with sandstone. Several types of bonding agents, including shellacs, rubbers and synthetic organic resins, are used to hold the abrasive particles together. There is little information available about the chemical composition or size of airborne particles which are generated during dry or wet grinding or during "dressing" with diamond cutting devices.

There are other chemicals of toxicologic concern which have been found as components or contaminants of cutting fluids but which have received little systematic study. These include polychlorinated biphenyls which may be present when lubricating oils or hydraulic fluids contaminate cutting fluid systems and para-tert-butyl benzoic acid, a reproductive toxin in animal tests, which has been used as an additive to soluble fluids,[27] and chlorinated oils and waxes recently found to be carcinogenic in rats and mice.[28]

In addition to the machining and grinding operations, there are other metalworking processes in bearing plants and similar facilities which may contribute hazardous exposures to the working environment. Smokes, oil mists and carbon monoxide may be generated in forging and heat treating operations when lubricating oils and cutting fluids are heated or burned. In forging, hot metal parts may be sprayed with heavy oil lubricants prior to pressing; in heat treating, red-hot parts may be quenched in heavy oil baths. Other potential exposures include chromic acid mists from electroplating operations and metal dusts such as beryllium or cadmium from grinding on specialty metals. Tool and die work in preparing the hard metal cutting tools includes grinding tungsten carbide and related special alloys. Cobalt and other exposures can result.

Health Effects

Animal Studies

Animal studies have demonstrated the carcinogenicity of several varieties of new and used cutting fluids as well as some of their specific components and contaminants.

A soluble and a straight cutting oil from a metalworking plant where skin cancers among workers were reported [29] were both found to cause skin cancer when applied repeatedly to the skin of mice.[30] In another study, a number of base stocks used in the preparation of cuttings oils were found to be carcinogenic to mouse skin.[18] Those oils conventionally refined with

sulfuric acid were carcinogenic, whereas solvent refined oils did not produce tumors. However, in a later study, solvent-extracted cutting oils were found to be carcinogenic as well.[31] This study also reported more papillomas in mice painted with used oil than with the same oil before use, suggesting the formation of carcinogens during industrial use. Mulligan has reported significant excess numbers of hepatic nodules in female mice which were skin painted with synthetic cutting fluids, both with and without measurable amounts of nitrosodiethanolamine.[32]

Both polycyclic aromatic hydrocarbons and nitrosamines have been shown to cause digestive[33,34] and respiratory[35] cancer in laboratory animals. N-nitrosodiethanolamine, the most frequently cited carcinogen found in synthetic cutting fluids, has potent effects in several animal species.[36,37,38] Nitrosodiethanolamine has also been found to be absorbed through rat skin when applied undiluted or in solution with water or cutting fluids.[39]

Female ICD-JCL mice exposed orally to triethanolamine developed a high incidence of malignant lymphomas in one study.[40] This has been questioned because of an unusually low rate of tumors in the control animals. Triethanolamine and diethanolamine are both currently being tested for carcinogenicity through the National Toxicology Program.[41] Formaldehyde has been shown in two studies to cause nasal cancers in rats.[42,43]

Neither aluminum oxide nor silicon carbide has been shown to induce tumors in animals. However, several respirable dusts, including sands, abrasives and metallic aerosols, have co-carcinogenic properties when given together with benzo(a)pyrene or diethylnitrosamine. Stenback found that neither aluminum oxide nor diethylnitrosamine produced lung tumors when given alone to Syrian Golden hamsters, but that significant numbers of lung tumors developed among hamsters pretreated with subcutaneous diethylnitrosamine followed by intratracheal aluminum oxide.[44] However, similar tumors also developed when 0.9 percent NaCl, used as the vehicle for the dust, was given with diethylnitrosamine but without the aluminum oxide.

Silica, chromite sand, olivine sand, ferric oxide and aluminum silicate dusts have all been found co-carcinogenic for lung tumors in hamsters when given with benzo(a)pyrene.[45] Stenback was not able to demonstrate co-carcinogenicity of aluminum oxide given to hamsters together with benzo(a)pyrene, although 2 of 48 animals developed lung adenomas which were not found when either material was administered alone.[46] Ferric oxide and titanium oxide had a marked co-carcinogenic effect in the same study.

Human Epidemiology: Occupational Groups

Early concern for the health of workers exposed to metalworking fluids and related chemicals focused on reports of dermatitis, skin cancer and non-malignant respiratory disease. Oil folliculitis has frequently been reported among those working with straight oils, while irritant and allergic contact dermatitis are the most frequent skin disorders associated with soluble and synthetic metalworking fluids (reviewed by Taylor).[47] Proliferative skin diseases, including keratoses and malignant tumors, have been found among

workers exposed to straight and soluble oils by direct skin contact or through oil impregnated clothing.[48] In Britain, this has been best documented for scrotal carcinomas and epitheliomas among workers exposed to straight oils and probably soluble oils (reviewed by Waterhouse).[49] A recent case-control study in Connecticut has demonstrated a similar association between squamous cell carcinoma of the scrotum and employment on metalworking jobs presumed to involve cutting fluid exposure (toolmakers, toolsetters, screw machine operators).[50]

Airborne mists from machining and grinding operations are known to contain droplets of respirable size (less than 5 um). Lipoid pneumonia and impairment of respiratory function have been reported among workers exposed to such respirable mist.[51] There is disagreement, however, about the prevalence and severity of these effects, and several investigators have failed to demonstrate respiratory dysfunction in coolant exposed workers.[52,53] In a recent cross-sectional evaluation of 164 bearing plant workers exposed to straight and soluble oil for a mean duration of 16 years, Jarvholm found a significant excess in respiratory symptoms relative to office worker controls.[16] He was unable to demonstrate differences in spirometric measures or x-rays.

Since 1970, several reports have linked cancers other than those of the skin with work in occupations or plants with cutting fluid exposures. In a population-based case-control study, Roush found a strong association between sino-nasal cancer mortality and jobs with presumed cutting fluid exposure.[54] In a similar study, Silverman demonstrated a slight association between bladder cancer mortality and metal fabrication and machinist work.[55]

The sino-nasal and bladder cancer findings are isolated reports, but several studies have found a relationship between cutting fluid mist exposure and cancers of the digestive and respiratory systems. Waterhouse reviewed 228 cases of scrotal cancer in oil mist exposed workers from the Birmingham Regional Cancer Registry and found significant excesses of subsequent primary malignancies of the skin, respiratory system and upper digestive tract.[56] Dubrow and Wegman reported associations between stomach, colo-rectal, pancreas, and respiratory cancers with work as machinists in Massachusetts, using age standardized mortality odds ratios.[57]

Decoufle calculated cause-specific standardized mortality ratios among workers on metal machining jobs in an engine plant.[5] There was a slight excess of respiratory cancer (38 observed, 33.9 expected) and digestive cancer (59 observed, 49.6 expected) for white males employed 5 or more years in oil mist exposed jobs. For those first employed before 1938 and with at least 20 years latency, there was a significant two-fold excess of cancer of the stomach and large intestine (15 observed, 7.6 expected). Although each of the three main classes of cutting fluids was used at the plant, no attempt was made to distinguish among exposures. A proportional mortality study of deaths among workers in an engine plant similar to that studied by Decoufle has also revealed significant excesses of lung and gastrointestinal cancers, particularly of the pancreas, among those with more than 20 years of employment.[58]

Of particular relevance is a cancer incidence study by Jarvholm in a Swedish bearing plant which is reported to be very similar to the plant in this investigation.[4] Among machining workers exposed to acid-refined mineral oils, there were four scrotal cancer cases but no excess in lung or digestive cancer. Among grinders who worked with soluble cutting fluids with nitrite additives and mineral oil contaminants, there was a statistically significant two-fold excess in digestive system cancer (15 observed, 7.8 expected) among those with more than 5 years of service and 20 years latency. There were 6 stomach cancers in this group, while 2.6 were expected. No excess of lung cancer was noted among grinders. Jarvholm has also reported a cluster of cancer cases (several sites) among women wrapping bearing rings covered with an antirust oil containing N-phenyl-1-naphthylamine.[59]

In a previous study by the UAW at a different bearing plant,[2] the major findings were statistically significant excesses in proportional mortality from stomach cancer (PMR=1.99), rectal cancer (PMR=3.07), and stroke (PMR=1.37) among white men. There was a strong association between stomach cancer and grinding exposures after control for age and country of birth. Other findings included excess lung cancer among women grinders, and an ill-defined syndrome diagnosed but probably misclassified as "chronic alcoholism" among grinders. There was an elevated PMR for cancer of the pancreas in grinding-exposed workers in this study (PMR=4/2.2=1.79) that was not statistically significant.

One study of a population exposed to oil mist reported no excess of cancer mortality;[52] however, the study group size and follow-up period were extremely limited.

Exposures to synthetic abrasives, which are potentially present in metal-working plants, have received far less epidemiologic attention than cutting fluids. Several reports, however, have recently appeared. Sparks found excess deaths from pancreatic cancer, stomach cancer, stomach ulcers and alcoholism in a proportional mortality analysis of 931 deaths among jewelry workers.[60] Other causes of death associated with alcoholism, such as cirrhosis and accidents, were not in excess. Stomach cancer and ulcers, but not pancreatic cancer or alcoholism, were elevated in the subgroup of polishers, presumed to experience exposure to abrasive dusts. Wegman found excess digestive cancer (stomach, esophagus, large intestine, rectum and liver) and non-malignant respiratory disease deaths in a proportional mortality analysis of 968 deaths among workers in a synthetic abrasive product manufacturing plant.[61] Conclusions could not be made about the association of cause-specific mortality with specific jobs or exposure. Jarvholm has reported a similar excess of digestive system cancer and non-malignant respiratory disease incidence in a group of workers employed in abrasive product manufacture,[62] and also a ten-fold risk of stomach cancer among bearing ring polishers using pastes containing waxes and abrasives.[63] Wang has reported excess standardized mortality odds ratios for colo-rectal and other disgestive cancers among workers manufacturing optical lenses and frames possibly exposed to abrasives and cutting fluids.[64] A role for abrasive dusts in stomach cancer etiology is supported by the finding of elevated stomach cancer SMRs in a cohort of British cement workers.[65] In the group with the likely highest exposure, the SMR exceeded 3.0 and was not accounted for by confounding due to social class.

Human Epidemiology: Other Factors

Nonoccupational factors in the epidemiology of stomach, colon and rectal cancer have received considerable attention. Stomach cancer incidence is strongly associated with ethnic background. Annual male age-adjusted incidence per 100,000 population ranges from the world's high of 91 among Japanese to a low of 10 among white U.S. men. Eastern European rates are in the mid-range, three to four times higher than U.S. rates.[66] Rates for Japanese migrants to the U.S. are intermediate between the rates for country of origin and destination.[67] However, rates for first-generation Polish migrants to the U. S. remain very close to the Polish rates.[68] Several investigators have argued that the Japanese pattern suggests a dietary effect,[67,69] and others contend that the Polish data suggest a genetic factor. The migrant findings have also not been analyzed with respect to changes in occupational and other environmental factors.

Stomach cancer rates have also been associated with the use of nitrate fertilizers in Chilean communities in one study and with the nitrate concentrations in public water supplies in another.[69]

In the U.S., stomach cancer incidence is greater among men than women and greater among blacks and hispanics than whites.[70] Among white males in the 1970s, stomach cancer incidence was somewhat higher in the Connecticut SEER area than in all the SEER areas combined (average annual age-adjusted incidence rates per 100,000 population of 14.3 and 12.7, respectively).[70]

The highest rates worldwide for colon and rectal cancer are in the U.S., particularly in Connecticut, and lowest in Japan. Eastern European rates are close to the low Japanese levels. Schottenfeld[71] points out that colon cancer incidence in Connecticut has increased 165 percent among white men and 192 percent among white women over the past 30 years, while rectal cancer incidence has remained stable. Colon cancer incidence is generally twice that of rectal cancer except in several Eastern European countries where the difference is much less marked and in some cases absent.[71]

The change in colon and rectal cancer incidence among migrants toward the rates of the country of destination is much more marked for these sites than for stomach cancer. Staszewski[68] notes that this effect is strongly apparent among Polish migrants. There has been considerable speculation that dietary factors influence the national differences and migrant patterns in cancer of the colon and rectum, with high risk possibly associated with diets high in fats and animal protein.

Patterns of cancer mortality are affected by alcohol consumption. Oropharyngeal, esophageal and liver cancer are clearly associated with heavy alcohol intake.[72] Associations between colo-rectal, pancreas and lung cancer have been reported, but the literature is inconsistent and the relationships are not considered well-established.[73] Although one recent study found a strong positive association between alcohol and stomach cancer mortality, most other studies have been negative or ambivalent.[74] Confounding by workplace exposures was not considered.

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DISCUSSION

Study Population

The specification of the candidate study population (cohort at risk) is believed to be quite complete, because the local union records were exceptionally well maintained; only 1.2 percent additional candidates were identified from the employer's pension record. Vital status ascertainment should be quite complete for those who died after age 65, when pension and social security systems are very likely to be informed of deaths. Former employees who had died by the time of the study closing date and who had not yet received any social security benefits are more likely to be lost. A rough estimate of the size of this group can be based on the distribution of the known deceased over year of birth. Workers born after 1917 would not have reached age 65 before the end of the study period. In fact, there is a drop in the numbers born per year from the 5-year period prior to 1917 to the following 5 years: from approximately 35 per year to 15 per year. There is a general trend downward over this period since only 12 members of the study population were born after 1927. Thus, perhaps 120 additional members of the candidate study population, less than 5 percent of the total, were in fact deceased and would have qualified for the study population (20 per year declining to 0 per year over the period 1917 to 1928).

Some deaths occurring in the years 1982-1983 may have been missed because the pension and social security sources did not fully cover that interval; the local union records were the only source on vital status for the last approximately eight months of the study period. Based on the the trend for numbers of deaths, annually, in the period 1978-1981, approximately 120 or less than 5 percent of total known deaths in the candidate study population may have been missed. Thus, the total deficit is believed less than 10 percent.

The use of a weighting procedure to adjust intervals of exposure duration (to reflect proximity in time to the date of death) was intended to discount the contribution of those with low potential risk of long latency work-related disease. Because this procedure incorporates latency effects into the duration variable, it has advantages over the common technique of fixing a minimum duration of employment and analyzing subgroups defined by duration intervals. Furthermore, on biological grounds it is more plausible to use a continuous function in addressing latency rather than a step function, as is done implicitly when, for example, a 15-year minimum exposure latency prior to death is used (equal weight for exposures earlier than 15 years prior to death; discounting all exposures subsequently).

Cause of Death

It is unlikely that misclassification arising from the use of transcripts has had any impact on the results, interpretation, or conclusions in this investigation. First, actual death certificates were obtained for all cases

involving outcomes of special interest and, second, for the 400 cases where both a certificate and a transcript were available, the veracity of the transcript was very high. Less than 10 percent of this group was discordant on the 3-digit ICD codes derived independently from certificate and transcript; most of the discordant pairs involved choices between non-malignant conditions of no consequence for this study.

Job Histories

The 6.3 percent of the study population lacking job history is probably largely comprised of relatively short-term employees whose employment interval fell between the dates of the seniority lists utilized and workers from the Meriden plant who quit by 1970, before appearing on a seniority list. Others missed may include women whose names changed (very few instances of this were found using pre-married names obtained from death certificates) or those with undetected name spelling changes or errors.

For employees whose employment interval fell largely within the period 1944-1972, mainly short-term job changes (i.e., less than two years) might have been missed using sampled seniority lists. The majority of the study population was hired before 1940; for them, the pre-1944 cumulative exposures based on extrapolation from the 1944-1972 period probably involve some misclassification. This is particularly true because World War II intervened in the course of most workers' job histories. This misclassification would result in underestimation of observed effects related to particular exposures. Also lacking in job history was any employment prior to or following employment at this bearing plant.

Because a worker's job history was specified for as many as seven points in time, the number of distinct exposure categories in which workers accrued work duration is an indication of the mobility across exposure categories. For 1,297, or 73 percent of the study population, the number of different exposure categories assigned was 1 or 2; for 8.3 percent, 4 or more distinct exposure categories were assigned. This indicates that moderate stability existed in this industrial population.

Exposure Identification

While seniority groups identified from seniority lists for the most part correspond to relatively homogeneous work activities, they were somewhat deficient for clearly separating grinding jobs from related assembly jobs, and for distinguishing grinding in oils vs. water-based cutting fluids. Many of these jobs are done in physical proximity to each other so that even correct identification does not allow clear exposure attribution. The fundamental basis on which exposures to oil- or water-based cutting fluids in grinding operations were distinguished was the assumption that oil-based cutting fluids were used largely in race grinding while water-based fluids were used in all types of grinding. However, according to historical accounts, there were frequent exceptions to this general pattern, exceptions that are not retrievable using

any available data source. There are many jobs or seniority groups where the worker had exposure to particular processes such as grinding, although not a grinding machine operator — e.g., many skilled trades, material handling or other support personnel. Finally, sampling seniority lists at four-year intervals allows undetected intervening exposures of up to four years' duration. Thus all findings should be interpreted recognizing that misclassification has caused a diffusion of attributable cases into non-causative exposure categories, thus diminishing observed effects.

Other Analytical Considerations

Information on some important potential confounders such as diet, smoking or alcohol use was unavailable. Origin of birth is a partial surrogate for some of these.

Standardized proportional mortality ratio (SPMR) analysis has the limitation of being conditional on death and thus giving no direct estimates of absolute risk of death for particular causes. Risk estimates for specific causes may be overestimates if ratios for other causes are low — for example, because of selection effects related to hiring practices. However, in this study, the PMR for all circulatory disease was 1.00, indicating that selection for healthy workers has not resulted in overestimates of malignancies by virtue of depressed circulatory disease. PMR for stroke, overall, was less than 1.0, as expected, but that for arterioslerotic heart disease was 1.10, a statistically signficant elevation (P=.002). The exposure group with the highest PMR for coronary heart disease was Machining, Oil Cutting Fluids (PMR=1.2, not significant). This elevation is difficult to interpret in relation to workplace, diet, smoking and selection risk factors, but implies that PMRs for other causes which are attributable to workplace exposures underestimate risks.

The SPMR and logistic regression SMOR analyses used the reference rates of the U.S. national population. SPMRs for colon cancer and stomach cancer would probably have been lower if Connecticut reference rates had been used, as state rates for these sites are higher than national rates.[70] The case-control analysis is not affected, relying as it does on internal reference populations. The logistic regression, in using the national rates, should not produce biased exposure effect estimates but, instead, would estimate the general study population SMOR relative to the national rates.

Logistic regression proved to be a considerably more powerful method than crude odds ratio analysis of 2x2 tables because: 1) the logistic regression took duration of exposure into account, whereas the crude odds ratio analysis excluded those of short duration and treated those of larger duration as all of the same risk; 2) the logistic regression controlled for age, year and origin confounding; 3) multiple exposures could be assessed simultaneously; 4) while fitting the exposure duration with an exponential dependence may not be very appropriate biologically over the full range of durations, it does result in a high emphasis on long duration and hence long latency exposures, as is appropriate for long latency diseases. In the case of malignancies, an

exponential time-dependence may even be appropriate as suggested by some animal and theoretical models of carcinogenesis.[75]

Major Findings: Digestive Diseases

There is a large, highly significant excess of digestive disease mortality in this study population, primarily in cancer of the stomach and pancreas. These excesses were observed using external reference populations (SPMR), internal (case-control), and both (SMOR), and after control for confounding by origin of birth.

Stomach cancer was associated with grinding exposures but not machining exposures. Other groups with elevated proportions of deaths due to stomach cancer included the machinist and tool grinder skilled trades and Assembly/Packing. Workers in the machinist and tool grinder categories can be exposed to cutting fluids and precision grinding activity in the normal course of their work.

Birth in Canada was observed to be a large risk factor for stomach cancer proportional mortality in both the SPMR and logistic regression analysis (adjusted OR=2.6). However, vital statistics for the Province of Quebec indicate that age-adjusted death rates for stomach cancer in that province are elevated by only 25-30 percent over the period 1965-73 compared with the rest of Canada[76]. This elevation is considerably smaller than that implied by the logistic regression results. This could be a consequence of one or two of the stomach cancer deaths among the Canadian-born (who in general were hired at an earlier date) possibly having early grinding experience not reflected in job histories since 1946. If so, this implies the Canadian birth effect is overestimated and the grinding effect underestimated. Evidence for this misclassification was also observed in the proportions of Canadian-born workers with any grinding duration in relation to their date of termination. For Canadian workers terminating 1950-1954, 12 out of 37 (.32) had any grinding experience. For the periods of termination 1955-59, 1960-64, and 1965-69, the respective proportions with grinding experience were .48 (14/29), .69 (27/39), and .56 (31/55).

The primary prior hypothesis to be tested in this study has been confirmed: stomach cancer proportional mortality is associated with grinding in cutting fluids. This finding replicates the results of a previous study in a similar plant.[2] Although the estimated elevation is slightly higher for mixed water- and oil-based cutting fluids, with greater statistical significance than for water-based cutting fluids, this difference is not testable with any certainty, and is confounded by the type of grinding. The types of grinding where oil-based cutting fluids were used (form or race grinding) may also have produced the greatest concentrations of water-based cutting fluid mists. The failure to observe a stomach cancer excess in the machining workers (in SPMR and SMOR analyses), who used straight oil cutting fluids, supports the conclusion that the stomach cancer excess is associated with water-based fluids. Alternate interpretations are that the association is with abrasives alone, or with oil-

based fluids but only in the presence of some other co-factor such as abrasive debris.

It was not possible to distinguish risks associated with exposure to the main groups of likely carcinogenic exposures in this population — nitrosamines, polycyclic aromatic hydrocarbons and synthetic abrasives. The speculation that nitrosamine exposure is a key carcinogen in machining and grinding environments has been based largely on the identification of nitrosamines in synthetic fluids. In this and other epidemiologic studies, however, the predominant fluids appear to have been straight oils and water emulsified oils ("soluble fluids"). Nitrosamine generation is plausible in the soluble fluids which may have used organic amines as emulsifiers and the nitrite anti-corrosion agent, but this has not been systematically studied.

Finding the most certain grinding effect using the broad definition of grinding may reflect misclassification in assigning exposure status, may be the result of considerable worker migration among a set of jobs related to grinding, or may simply reflect the smaller numbers in the more specific groups. Another possibility is that the carcinogenic exposure is in fact dispersed more widely than simply splash and mist generation at grinding machines. Of the 18 stomach cancer deaths in workers with any cumulative duration in Grinding, Comprehensive, 9 were workers whose job exposure category of longest duration was grinding operator (jobs 8,11,12,13) and 4 were grinding inspectors (job 14). The proportion who were inspectors (4/(9+4)=.30) is greater than in the general population (all causes of death; 88/(323+88)=.21), suggesting a more general exposure than just at grinding machines. For example, anti-corrosion oils are used throughout metalworking areas where water-based cutting fluids pose a constant corrosion threat. One report in the literature found a carcinogenic hazard from one such oil.[59]

The association of cancer of the pancreas with machining and grinding is the second major finding. The strongest association was found for machining in oil, a relatively well-defined exposure category in that machining on multi-spindle lathes was a distinct category on seniority lists over the entire job history period, and has always been done in oil. The concurrent finding of an association with grinding, broadly defined, but only for workers whose date of hire came before 1933, suggests that the relevant exposure there was mineral oil cutting fluids as well, because straight oils began to be replaced by soluble oil cutting fluids in grinding in the 1930-40s. However, because work histories for the period prior to 1946 were based on extrapolation from those subsequent to that time, conclusions concerning workers with early dates of hire (e.g. 1920s) are necessarily tentative. Nevertheless, three of the nine pancreatic cancer cases in grinders had hire dates prior to 1920, and the mean hire date for these nine grinders was 1925, while the mean hire date for all grinders not dying of digestive cancer was 1930. This supports the inference that exposures to early, probably acid-refined mineral oils, may have been the cause of the pancreatic cancer in grinders. While solvent-refining of lubricating oils has been reported to reduce their carcinogenic potential and such refining now has largely replaced earlier acid-refining, nevertheless the cancer of the pancreas excess in this study gives no indication of a downward trend over hypothesized a priori, although earlier and subsequent reports in the literature

show there have been other indications of excess pancreatic cancer in metalworking populations.[2,58,60]

The model for colon cancer showed a dependence on birth in the U.S. with an odds ratio of 1.6. This effect is probably a consequence of using national reference rates; Connecticut colon cancer incidence is higher than national colon cancer rates and has been rising for a number of years.[71] This analysis suggests that the increase is limited to U.S. born.

There were excess proportions of deaths from cirrhosis of the liver among both white men and white women which were not statistically significant. Among the men, these excesses were present in most grinding subgroups, but only the group with 10 or more years of grinding in water/oil fluids sustained a significant increase in cirrhosis (PMR=5/1.5=3.27, p=.04). Case-control analysis also revealed the same significant finding when crude odds ratios were calculated (OR=3.01, p=.05); however, the magnitude and strength of the associations between non-malignant digestive diseases and grinding exposures dropped considerably with logistic regression. Although all 10 women dying of cirrhosis held assembly or inspection jobs in grinding areas, it is impossible to conclude anything about job-specific risk because 89 percent of women in the plant held assembly and inspection jobs.

Liver cirrhosis is strongly linked with alcoholism in this society, yet in this study group there was no excess mortality from alcoholism (only four deaths) or from most other causes associated with alcoholism (accidents, suicide, cardiomyopathy, oropharyngeal cancer). There was a small, non-significant proportional excess in mortality from one cause, esophageal cancer, which has been associated with alcoholism. Proportional mortality from liver cancer was elevated in several exposure subgroups, but numbers were quite small.

Other mortality studies in similar working populations exposed to cutting fluids and/or abrasives have found increased mortality from alcoholism but not from cirrhosis or other alcohol related diseases[2,60]. These inconsistencies in the mortality patterns, both within and among these various studies, strongly suggests errors in the identification of underlying cause of death. It is plausible, perhaps probable, that death certificates are unreliable indications of either alcoholism or liver disease unless they have been filled out by attending physicians thoroughly familiar with the decedent's medical history. In the absence of such knowledge, a medical examiner or a physician who only treated the patient briefly prior to death might be inclined to make a diagnosis of cirrhosis or alcoholism based on general findings suggestive of hepatic disease such as jaundice or a palpable, firm liver. Non-alcoholic, chronic liver disease might thus be misclassified simply because it is atypical and therefore unexpected. Support for this type of diagnostic bias was noted in the bearing plant study which is a companion to the current investigation.[2] In that study there was a large excess in "alcoholism" deaths, all 12 of which had been given by medical examiners as the cause of death. In the present study the death certificates for the cirrhosis of the liver deaths occurring in grinding were almost all filled out by attending physicians (14/15).

Non-alcoholic chronic liver disease has been associated with a wide variety of toxic agents in the environment and on the job. Pransky, for

example, reports such illness among refrigeration engineers, chemists, drycleaners, rubber manufacturers and workers exposed to tetrachloroethane and plutonium.[77] More directly relevent to this investigation are reports of the hepatotoxic effects of chronic and acute exposure to high doses of nitrosamines.[78,79] The possibility that cutting fluids and/or abrasives exposures can cause chronic liver disease requires further investigation. It is unlikely that this can be done in mortality studies unless there is access to medical records and autopsy reports.

Lung Disease

Based on SPMR and crude mortality odds ratio analyses, there was no statistically significant elevation in lung cancer, although in the exposure group exposed to oil smokes — forge, heat treat, heading and annealing -- there was a 50 percent increase in proportional mortality. The SMOR analysis, in contrast, produced a statistically significant association between duration in forge, heat treat exposures and lung cancer (odds ratio=2.0, 25 years exposure, p=.035). Another relevant exposure in this group was silica dust from descaling operations. Because the reference rates covered the period 1950 to 1980, while study deaths occurred into 1983, and because lung cancer rates are increasing, the estimate of the study population SMOR for lung cancer is a little larger than it should be; however, the exposure effect estimate should not be significantly affected. This finding supports the prior hypothesis that lung cancer is elevated in this exposure group.[2,80]

Most exposure groups had SPMRs for non-malignant respiratory disease considerably smaller than 1.0, as expected for an industrially employed population free of inhalation hazards. The main exception was grinding in water/oil (believed to have the highest exposure to water- and oil-based cutting fluid mists), but the excess (PMR=1.36) was not statistically significant. Case-control analysis, comparing grinding with other jobs believed not to carry respiratory disease risks, produced a crude mortality odds ratio of 1.6, also not statistically significant. However, this finding is consistent with a similar pattern in another bearing plant.[2] A parallel excess of stroke was also observed in these two studies for grinding exposures, although the previous study showed a general excess of stroke in many job categories that was unexplained. No such general excess was seen in this study.

Cancer of the Lymphopoietic System

Tool and die workers and tool grinders experienced an unusually large proportion of deaths due to lymphopoietic cancers (PMR=9/1.84=4.89, p=.003). No other group had a similar elevation. This was not a hypothesized effect. The sites of cancer were primarily leukemia (four cases), lympho- or reticulosarcomas (two cases) and "other lymphatic cancers" (two cases). This pattern suggests no particular etiology. Solvent use by this group of workers may distinguish them from others. This finding merits further investigation into the history of this work at the study plant.

CONCLUSIONS AND RECOMMENDATIONS

1. This study provides strong support for previous findings of excess stomach cancer proportional mortality among workers in plants where metal machining and abrasive grinding are major activities. It confirms an association of stomach cancer with grinding jobs and with water-soluble cutting fluids. The consistency of several epidemiologic investigations makes it very likely that the observed association is causal. Additional epidemiologic investigations accompanied by thorough industrial hygiene evaluations are needed in order to examine possible associations between health outcomes and specific chemical exposures. Current and historic patterns of cutting fluid and abrasive use have not been adequately documented and require both qualitative and quantitative examination. Particular attention should be directed to identifying potential exposures to nitrosamines, polycyclic aromatic hydrocarbons, abrasive particulates, formaldehyde, and other organic volatiles. The effects of mixed or sequential exposures should be considered along with determinations of the physical and chemical properties of particulates, such as particle size and surface absorption characteristics, generated by various manufacturing processes.

2. This study also supports previous findings of increased proportional mortality for cancer at digestive system sites in addition to stomach. The strongest findings are for pancreatic cancer, with statistically significant increases among men with both grinding and machining jobs. The positive relationship between pancreatic cancer with duration in jobs using straight oil cutting fluids is evidence for occupational causation. These findings require further elaboration.

3. Other mortality studies in the bearing and related industries have been inconsistent with respect to possible lung cancer excesses. In this study, as with the prior companion bearing plant study,[2] there was no overall lung cancer excess nor an association of lung cancer with the machining and grinding jobs most likely to produce cutting fluid and abrasive exposures. However, the prior study suggested a disproportionate number of lung cancer deaths among decedents from forging and heat treat jobs. In this study there was an adjusted odds ratio for lung cancer of 2.0 ($p=.04$) for 25 years duration in these jobs among white men. This finding cannot stand on its own; there have been no other published reports of mortality among forging workers. However, there has been concern expressed about the effects of exposures to potential carcinogens generated by the pyrolysis of lubricants and quenching oils during forging activities.[80] The hypothesis that forge, heat treating and related work is associated with lung cancer strongly warrants more substantial investigation.

4. Several other findings are considered more tentative and require further validation:

a. Excess chronic liver disease proportional mortality, possibly associated with grinding exposures and possibly misclassified on death certificates as cirrhosis (or alcoholism[2]).

b. An association between liver cancer and machining exposures common to tool and die, machinist and production machining work.

c. An association between lymphopoietic cancers and tool and die exposures.

5. This study did not provide support for prior findings[2] of increased proportional mortality from rectal cancer among white men in bearing plants. There was a weak indication of increased stroke similar to a prior finding.[2]

6. Despite the need for further study, the present findings confirm the necessity of stringent measures to control exposures to cutting fluid and abrasive aerosols in this industry as a prudent public health measure. Until such time as scientific investigations are able to distinguish risks associated with specific metalworking processes, chemical exposures or levels of exposure, cutting fluid mists and related aerosols should be reduced to the lowest feasible level. Design, installation and maintenance of local exhaust ventilation systems for grinding and machining operations need to be improved to capture airborne particulates and organic volatiles. Wheel dressing procedures (shaping grinding surfaces with diamond), which are typically done at the grinding machine, with or without lubricant, deserve special attention.

In addition to ventilation, other methods should be employed to reduce the generation and exposure to known and suspected carcinogens in cutting fluid environments. Splash guards should be installed whenever possible and maintained in good repair. The force and direction of coolant streams should be adjusted frequently to reduce mist generation. The speed and pressure at metal-tool interfaces should be kept as low as possible to reduce frictional heat and particle dispersion. A priority should also be placed on maintaining low levels of known and suspected carcinogens in circulating cutting fluids; conditions for nitrosamine formation should be eliminated; biocide use should be reduced in favor of other means to curtail microbiologic growth. There is a particular need to reduce skin contact with cutting fluids, especially synthetic fluids, because of the ability of nitrosamines to penetrate human skin.[22,23]

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Figure 1

Sources and Selection of Study Population

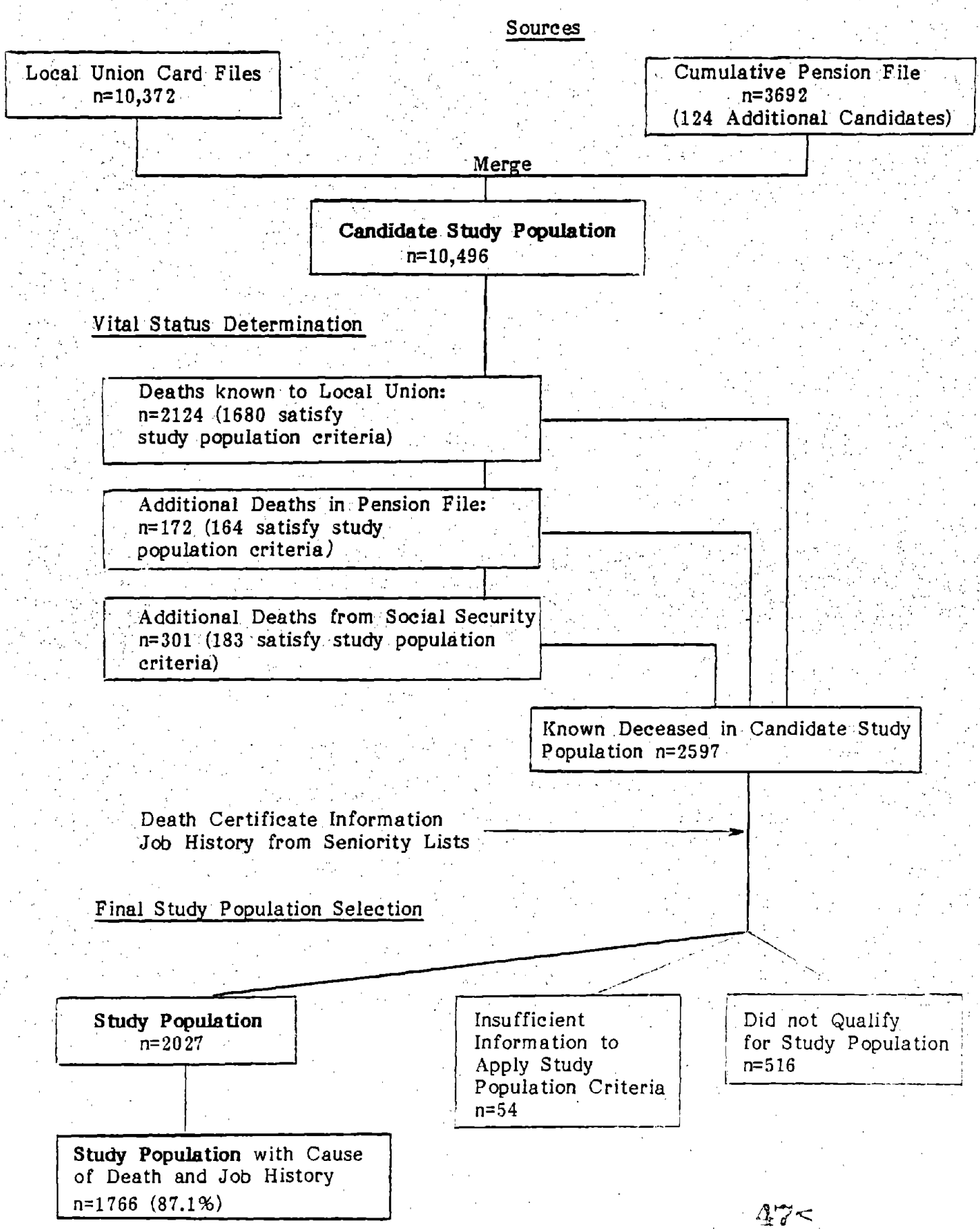

Table 1

Cause of Death Ascertainment in Relation to Vital Status Derivation

Vital Status	Study Population	Study Population with Cause of Death	
			%
Known Dead in Local Union Records	1680	1584	94.3
Known Dead in Pension File but not in Local Union Records	164	152	93.3
Known Dead in Social Security Files but not in Local Union or Pension File	183	142	77.6
Total	2027	1878	92.6

Table 2

Exposure Categories Defined for Bearing Plant

TITLE	JOB EXPOSURE NO.
FORGE	01
HOT/COLD HEADING	02
MACHINING (OIL CF)	03
MACHINING (WATER CF)	04
MACHINING (UNKNOWN OR MIXED CF)	05
MACHINING (SECOND, OIL CF)	06
MACHINING,GREY IRON	07
FILING	08
HEAT TREAT,RINGS	09
HEAT TREAT,BALLS	10
GRINDING (OIL CF)	11
GRINDING (WATER CF)	12
GRINDING (UNKNOWN OR MIXED CF)	13
GRINDING,INSPECTION	14
PLATING	15
LAPPING	16
HONING	17
POLISHING	18
STAMPING;PUNCHING;RETAINER MACHINING	19
LABORATORY: CHEM.,METALL.	20
WHEELMAKING	21
TOOL GRINDING(PRODUCTION)	22
ASSEMBLY;GAGING;PRESSING;SALVAGE	23
PACKING	24
SHIPPING;INVENTORY;STORAGE;MAT.CTL;MISC.	25
INSPECTION,BALLS,FINAL	26
SKILLED TRADES,ELECTRICIANS(MAINTENANCE)	27
SKILLED TRADES,MACHINISTS(MAINTENANCE)	28
SKILLED TRADES,OTHER;(MAINTENANCE)	29
MILL SUPPLY	30
PRODUCTION CONTROL(STOCK HANDLING)	31
TUMBLING	32
CLEANER,BEARING PARTS	33
STEEL HANDLER	34
QUALITY CONTROL,STANDARDS CHECKING	35
ANNEALING & PICKLING	36
FOUNDRY,BRONZE	37
TRUCKING,GARAGE	38
SKILLED TRADES,MILLWRIGHTS;(MAINTENANCE)	39
SKILLED TRADES,PLUMBERS & PIPEFITTERS(MAINT.)	40
BATTERY CHARGING	41
BOILER HOUSE	42
PATTERN MAKERS	43
PRINTING PRESS	44
LAUNDRY	45
OILERS	46
BALL SHOP,MIXED	47
SKILLED TRADES,BRICKLAYERS;(MAINTENANCE)	48
MAINTENANCE(NON-SKILLED)	49
TOOL & DIE MAKERS	50

Table 3

Sample of Seniority Groups Identified from Seniority Lists with Assigned Exposure Category [1]

SEN.GROUP	EXPOSURE NO.	SENIORITY GROUP TITLE
Seniority List of 1946		
104	01	FORGE SHOP-OILERS
111	09	FORGE SHOP-DIE & TOOL HARDENING
100	01	FORGE SHOP-MISC.
400	03	AUTOMATIC DEPT.-MALE
503	12	GRINDING & ASSEMBLY-O.D. GRIND
507	11	GRINDING & ASSEMBLY-CUP BALL RACE
512	23	GRINDING & ASSEMBLY-FEMALE, ALL
577	24	GRINDING & ASSEMBLY-ASSEMBLY & PACKING
604	08	BALL SHOP-ROUGH BALL GRIND, SMALL BALL
606	50	BALL SHOP-DIE DEPT.
800	25	SHIPPING
906	39	PLANT ENG.-MILLWRIGHT
929	49	PLANT ENG.-SWEEPERS & PORTERS
1403	28	MECHANICAL-MACHINING
1411	39	MECHANICAL-MACHINE ASSEMBLY & REPAIR
1504	21	PURCHASING-WHEEL ROOM
Seniority Lists of 1950,1954		
1	01	FORGE SHOP-FORGING-MALE
15	36	FORGE SHOP-ANNEALING-MALE
20	03	MACHINING-BAR-MALE
25	04	MACHINING-LATHES-MALE
75	02	BALL SHOP-HEADING
100	12	GRINDING & ASSEMBLY-BORE
105	12	GRINDING & ASSEMBLY-SURFACE
115	11	GRINDING & ASSEMBLY-BALL RACE
120	23	GRINDING & ASSEMBLY-ASSEM.
125	31	GRINDING & ASSEMBLY-GENERAL
200	23	PRESS-FEMALE
205	23	GRINDING&ASSEM.-FEMALE
230	14	INSPECT.-GRND.&ASSEM.-MALE
375	28	MECHANICAL-MACHINISTS-MALE
400	28	MECHANICAL-BALL PLATE MACHINING
430	23	MECHANICAL-GAUGE & APPLIANCE-FEMALE
Seniority Lists of 1958,1962,1966,1970		
1	01	FORGING
20	03	MACHINING-BAR
25	04	MACHINING-LATHE
40	11	GRINDING & ASSEMBLY
50	47	BALL SHOP-HEADING,GRINDING,GAUGING
55	12	PRESS,PLATING,GRINDING;PERFEX
105	01	PLANT ENG.-BLACKSMITH
125	27	PLANT ENG.-ELECTRICIANS
190	50	MECHANICAL-TOOL AND DIE
195	28	MECHANICAL-MACHINISTS
200	12	MECHANICAL-GRINDERS
230	22	MECHANICAL-CARBIDE TOOL GRINDERS
245	50	MECHANICAL-GAUGE & APPLIANCE

1. A sample of 283 distinct Seniority Groups.

Table 4

Selected Values of Weighting Function Used in Calculation of Cumulative Exposures

Weighting Function[1]	Time of Exposure (t) in Years Prior to Death[2]								
	30	25	20	15	12.5	10	7.5	5	2.5
w(t)	.999	.993	.953	.731	.500	.269	.119	.049	.018

1. $w(t) = (1 + e^{.4(12.5 - t)})^{-1}$, a cumulative logistic distribution.

2. Period from mid-point of exposure interval until death.

Table 5

Distribution of White Men in Study Population in Major Exposure Categories Used in SPMR Analyses

Exposure Variable[2]	Duration in Exposure[1] (Mos.) Less than 40 n	%[2]	40-119 n	%	120 or More n	%	Job Categories
Machining							
All CF	1263	82.4	111	7.2	158	10.3	3-5
Oil CF	1341	87.5	127	8.3	64	4.2	3
Water CF	1453	94.8	59	3.9	20	1.3	4
Grinding							
Comprehensive	972	63.4	210	13.7	350	22.8	8,11-14,31
Restrictive	1209	78.9	130	8.5	193	12.6	11-13
Water/Oil CF	1341	87.5	86	5.6	105	6.9	11
Water CF	1385	90.4	77	5.0	70	4.6	12
Forge and Heat Treat	1328	86.7	73	4.8	131	8.6	1,2,9,10,36
Tool and Die	1399	91.3	52	3.4	81	5.3	50
Tool Grinding	1460	95.3	20	1.3	52	3.4	22
Machinist	1449	94.6	35	2.3	48	3.1	28
Assembly, Packaging	1323	86.4	83	5.4	126	8.2	23-26,30,35

1. Cumulative exposure duration has been weighted according to interval prior to death; see Methods.

2. See p. 10 for definition of exposure groups.

Table 6

Construction of Exposure Variables for Use in Case-Control Studies (Crude Mortality Odds Ratios)

EXPOSURE VARIABLE	JOB EXPOSURE CATEGORIES		PRIMARY OUTCOME TESTED
	EXPOSED	EXCLUDED	
MACHINING,ALL CF	03,04,05	08,11,12,13,14,22,28,34,43,50	CA OF COLON
MACHINING,OIL CF	03	04,05,08,11,12,13,14,22,28,34,43,50	CA OF COLON
MACHINING,WATER CF	04	03,05,08,11,12,13,14,22,28,34,43,50	CA OF COLON
GRINDING,COMPREHENSIVE	08,11,12,13,14,31	22,32,33,43,47,50	CA OF STOMACH, NMDD
GRINDING,RESTRICTIVE	11,12,13	08,14,22,31,32,33,43,47,50	CA OF STOMACH, NMDD
GRINDING,OIL CF	11	08,12,13,14,22,31,32,33,43,47,50	CA OF STOMACH, NMDD
GRINDING,WATER CF	12	08,11,13,14,22,31,32,33,43,47,50	CA OF STOMACH, NMDD
GRINDING,COMPREHENSIVE	08,11,12,13,14,31	01,02,09,10,15,21,22,32,33,36,40,41,47,49	CA OF LUNG
GRINDING,RESTRICTIVE	11,12,13	01,02,08,09,10,14,15,21,22,32,33,36,40,41,47,49	CA OF LUNG
GRINDING,OIL CF	11	01,02,08,09,10,12,13,14,15,21,22,32,33,36,40,41,47,49	CA OF LUNG
GRINDING,WATER CF	12	01,02,08,09,10,11,13,14,15,21,22,32,33,36,40,41,47,49	CA OF LUNG
TOOL AND DIE: ALL	22,50	03,04,05,43	CA OF RECTUM
TOOL GRINDING ONLY	22	03,04,05,43,50	CA OF RECTUM
TOOL AND DIE: ALL	22,50	08,11,12,13,14,31,43,47	CA OF STOMACH
TOOL GRINDING ONLY	22	08,11,12,13,14,31,43,47,50	CA OF STOMACH
FORGE,HEAT TREAT	01,02,09,10,22,36	08,11,12,13,14,15,31,40,41,47,49,50	CA OF LUNG
TUMBLING,PARTS CLEANING	14,31,32,33	01,02,09,10,11,12,13,36,43	NMRD

1 NMDD - non-malignant digestive disease; NMRD - non-malignant respiratory disease.
2 Case-control comparison group: all those whose aggregate time in the 'exposed' and 'excluded' job categories was less than 12 months.

Table 7

Construction of Outcome Variables Used in Case-Control Analysis (Crude Odds Ratios)

Outcome	ICD Coded Underlying Cause of Death			Primary Exposures of Interest
	Case	Control	Excluded	
Stomach Cancer	151	1-149, 170-289, 318-459, 578-999	150, 152-163, 290-317, 460-577	Grinding, Tool & Die
Colon Cancer	153	1-149, 170-519, 578-999	150-152, 154-163, 520-577	Machining
Cancer of Rectum	154	1-149, 170-459, 520-999	150-153, 155-163, 460-519	Tool & Die
Cancer of Pancreas	157	1-149, 170-289, 318-459, 520-999	150-156, 158-163 290-317, 460-577	Grinding, Machining
All G.I. Cancer	150-519	1-149, 170-289, 318-518	160-163, 290-317, 519-577	Grinding, Machining, Tool & Die
Cancer of Lung	162	1-149, 170-459, 520-999	160-161, 163, 460-519	Forge, Heat Treat
Cancer of Lung	162	1-149, 170-289, 318-459, 520-999	150-161, 163, 290-317, 460-519	Grinding
Lymphopoietic Cancer	200-209	1-149,160-199, 210-999	150-159	Tool Grinding, Tool and Die
Non-Malignant Respiratory Disease[1]	491-519	1-150, 152-159, 170-199,201, 202-207, 209-999	151, 160-163, 200, 202, 203, 208	Grinding
Non-Malignant Digestive Disease	520-577	1-149, 170-289, 318-459, 578-999	160-163, 290-317, 460-519	Grinding
Cirrhosis of Liver	571	1-149, 170-459, 578-999	150-163, 460-570, 572-577	Grinding

1. Includes: chronic bronchitis, emphysema, interstitial lung diseases, chronic obstructive lung disease.

Table 8

Ascertainment of Job History and Cause of Death in Study Population[1]

	Study Population		Study Population With Job History		Study Population with Cause of Death		Study Population with both Job History and Cause of Death	
		%		%		%		%
Total	2027	100.	1898	93.6	1878	92.6	1766	87.1
White Men	—		—		1616		1532	
White Women	—		—		243		220	
Non-White Men	—		—		12		12	
Non-White Women	—		—		5		2	

1. Sex and Race not reliably known for study population without cause of death (death certificate) information.

Table 9

Distribution of White Men in Study Population by Age of Hire, Age at Death and Year of Death and by Origin of Birth

		Origin of Birth									
		U.S.		C. Europe		Canada		Other		Total[1]	
		n	%	n	%	n	%	n	%	n	%
Age at Hire	15-	495	52.1	46	26.1	78	48.4	45	19.2	664	43.6
	30-	270	28.4	64	36.4	52	32.3	92	39.3	478	31.4
	40-	145	15.2	45	25.6	24	14.9	61	26.1	275	18.1
	50-	39	4.1	19	10.8	7	4.3	35	15.0	100	6.6
	60+	2	.2	2	1.1	0		1	.4	5	.3
Age of Death	30-	131	13.8	3	1.7	13	8.1	3	1.3	150	9.9
	55-	291	30.6	23	13.1	28	17.4	23	9.8	365	24.0
	65-	304	32.0	62	35.2	65	40.4	72	30.8	503	33.0
	75+	225	23.7	88	50.0	55	34.2	136	58.1	504	33.1
Year of Death	1950-	109	11.5	40	22.7	35	21.7	45	19.2	229	15.0
	1960-	275	28.9	75	42.6	46	28.6	86	36.7	482	31.7
	1970-	438	46.1	57	32.4	66	41.0	90	38.4	651	42.8
	1980+	129	13.6	4	2.3	14	8.7	13	5.5	160	10.5
	Total	951		176		161		234		1522	
	%	62.3		11.6		10.6		15.4		100.	

1. 10 cases missing origin of birth information.

Table 10

Distribution of White Men in Study Population by Origin of Birth Within Exposure Categories of Longest Duration[1]

Origin[2] of Birth	Forge		Heat Treat		Machining		Grinding		Tool & Die		Tool Grind		Machinist		Assembly Pkg.		Other Skilled		Total[3]	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
U.S.	63	66.3	32	47.1	119	58.9	286	64.0	79	80.6	30	66.7	54	80.6	96	65.3	110	67.5	951	62.1
C. Europe	12	12.6	15	22.1	34	16.8	46	10.3	4	4.1	4	8.9	5	7.5	12	8.2	6	3.7	176	11.5
Canada	11	11.6	4	5.9	23	11.4	58	13.0	3	3.1	6	13.3	0		19	12.9	13	8.0	161	10.5
Italy	3	3.2	11	16.2	14	6.9	32	7.2	1	1.0	1	2.2	2	3.0	10	6.8	11	6.7	114	7.4
Other	6	6.3	6	8.8	12	5.9	25	5.6	11	11.2	4	8.9	6	9.0	10	6.8	23	14.1	120	7.8
Total	95		68		202		447		98		45		67		147		163		1532	
%	6.2		4.4		13.2		29.2		6.4		2.9		4.4		9.6		10.6			

. Cumulative exposure duration has been weighted according to interval prior to death; see Methods.
. 9 cases missing origin of birth information.
. Includes 191 in other job categories not presented.

Table 11

Distribution of White Men in Study Population by Age of Hire, Age at Death and Year of Death Within Exposure Categories of Longest Duration[1]

		Forge		Heat Treat		Machining		Grinding		Tool & Die		Tool Grind		Machinist		Ass'y/ Pkg.		Total[2]	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Age at Hire	15-	42	44.2	25	36.8	86	42.4	236	52.4	44	44.4	20	44.4	29	43.3	79	53.0	667	43.5
	30-	41	43.2	22	32.4	60	29.6	128	28.4	35	35.4	18	40.0	13	19.4	50	33.6	483	31.5
	40-	8	8.4	19	27.9	41	20.2	59	13.1	18	18.2	6	13.3	20	29.9	15	10.1	277	18.1
	50-	4	4.2	2	2.9	15	7.4	25	5.6	2	2.0	1	2.2	5	7.5	5	3.4	100	6.5
	60+	0		0		1	.5	2	.4	0		0		0		0		5	.3
Age at Death	30-	8	8.4	6	8.8	25	12.3	58	12.9	9	9.1	3	6.7	2	3.0	18	12.1	151	9.8
	55-	24	25.3	9	13.2	54	26.6	113	25.1	24	24.2	9	20.0	22	32.8	39	26.2	368	24.0
	65-	42	44.2	33	48.5	62	30.5	137	30.4	38	38.4	16	35.6	18	26.9	50	33.6	504	32.9
	75+	21	22.1	20	29.4	62	30.5	142	31.6	28	28.3	17	37.8	25	37.3	42	28.2	509	33.2
Year of Death	1950-	19	20.0	13	19.1	39	19.2	40	8.9	18	18.2	8	17.8	1	1.5	20	13.4	230	15.0
	1960-	35	36.8	29	42.6	66	32.5	151	33.6	31	31.3	13	28.9	16	23.9	44	29.5	487	31.7
	1970-	31	32.6	17	25.0	78	38.4	213	47.3	37	37.4	24	53.3	43	64.2	62	41.6	654	42.7
	1980+	10	10.5	9	13.2	20	9.9	46	10.2	13	13.1	0		7	10.4	23	10.3	161	10.5
	Total	95		68		203		450		99		45		67		149		1532	

1. Cumulative exposure duration has been weighted according to interval prior to death; see Methods.
2. Includes 356 in other job categories.

Table 12

Comparison of Conflicting Causes of Death Coded from Death Certificates and Transcribed Death Certificates

	Transcript	Certificate	Age	Year	ICD Version
	First Subset (selected for coding complexity)				
1	151.9	150.0	83	75	8
2	185.0	151.0	64	65	7
3	185.0	410.0	88	60	7
4	185.0	480.0	75	56	6
5	191.0	210.0	46	57	6
6	197.0	153.0	73	58	7
7	197.0	174.0	62	52	6
8	197.0	174.0	63	62	7
9	202.0	204.3	75	63	7
10	290.0	571.0	37	55	6
11	410.0	250.0	62	56	6
12	450.0	410.0	54	58	7
13	480.0	493.0	47	51	6
14	553.3	533.1	68	74	8
15	572.0	430.0	59	57	6
16	782.0	850.0	52	57	6
	Second Subset (selected for G.I. or lung CA, or cirrhosis)				
1	90.0	450.0	65	55	6
2	153.0	154.0	64	72	8
3	153.0	197.0	52	67	7
4	153.8	440.9	72	68	8
5	250.0	400.0	76	55	6
6	250.9	571.0	43	70	8
7	410.0	393.0	55	52	6
8	410.0	493.0	62	50	6
9	410.9	571.9	54	70	8
10	412.3	410.9	62	81	8
11	412.3	433.9	69	68	8
12	419.0	400.0	83	53	6
13	419.0	400.0	80	56	6
14	419.0	500.0	73	52	6
15	490.0	500.0	67	53	6
16	534.0	540.0	42	51	6
17	571.0	486.0	54	68	8
18	571.0	880.0	63	60	7
19	890.0	830.0	36	54	6
20	890.0	830.0	44	54	6

All ICD codes given in ICD-8.

Table 13

Standardized Proportional Mortality Ratios for Selected Causes of Death in All White Men of Study Population (5 or More Years Duration of Employment)[1]

CAUSE OF DEATH	OBS	EXP	PMR	95% CI	CHI SQ	P
TOTAL DEATHS	1532					
ALL MALIGNANT NEOPLASMS	342	300.67	1.14	1.04, 1.25	7.16	.01
CANCER OF DIGESTIVE ORGANS AND PERITONEUM	137	90.16	1.52	1.29, 1.79	25.90	<.001
CANCER OF ESOPHAGUS	13	7.11	1.83	1.07, 3.12	4.91	.03
CANCER OF STOMACH	35	17.74	1.97	1.43, 2.72	17.01	<.001
CANCER OF LARGE INTESTINE	41	29.56	1.39	1.03, 1.88	4.52	.04
CANCER OF RECTUM	14	10.28	1.36	0.81, 2.29	1.36	
ALL CANCER OF LIVER - PRIMARY ONLY	9	6.66	1.35	0.71, 2.59	0.82	
CANCER OF PANCREAS	24	16.79	1.43	0.96, 2.12	3.13	.08
ALL CANCER OF LUNG - PRIMARY AND SECONDARY	83	90.47	0.92	0.75, 1.13	0.67	
CANCER OF SKIN	4	4.37	0.92	0.25, 2.34		
CANCER OF PROSTATE	29	29.03	1.00	0.70, 1.43	0.0	
CANCER OF TESTIS	0	0.82	0.00	0.00, 3.65		
CANCER OF BLADDER	14	11.09	1.26	0.75, 2.13	0.77	
CANCER OF KIDNEY	9	6.94	1.30	0.68, 2.48	0.61	
CANCER OF BRAIN AND OTHER CENTRAL NERVOUS SYSTEM	6	6.08	0.99	0.44, 2.19	0.0	
ALL LYMPHOPOIETIC CANCER	27	26.14	1.03	0.71, 1.50	0.03	
LYMPHOSARCOMA AND RETICULOSARCOMA	6	5.42	1.11	0.50, 2.46	0.06	
LEUKEMIA	12	10.89	1.10	0.63, 1.94	0.11	
CANCER OF OTHER LYMPHATIC TISSUE	6	7.01	0.86	0.39, 1.90	0.15	
ALLERGIC,ENDOCRINE,METABOLIC,NUTRITIONAL DIS.	26	26.13	1.00	0.68, 1.46	0.0	
MENTAL,PSYCHONEUROTIC,AND PERSONALITY DISORDERS	7	5.68	1.23	0.59, 2.58	0.31	
ALL DISEASES OF NERVOUS SYSTEM AND SENSE ORGANS	7	10.57	0.66	0.32, 1.38	1.21	
ALL DISEASES OF CIRCULATORY SYSTEM	881	883.86	1.00	0.96, 1.04	0.02	
ARTERIOSCLEROTIC HEART DISEASE,INCLUDING CHD	650	589.09	1.10	1.04, 1.17	10.27	.002
ALL VASCULAR LESIONS OF CNS	118	136.27	0.87	0.73, 1.03	2.73	.10
ALL RESPIRATORY DISEASES	94	103.73	0.91	0.75, 1.10	0.98	
ALL PNEUMONIA	37	38.52	0.96	0.70, 1.32	0.06	
EMPHYSEMA	20	24.94	0.80	0.52, 1.24	1.00	
ASTHMA	3	3.33	0.90	0.19, 2.63		
ALL DISEASES OF DIGESTIVE SYSTEM	76	61.54	1.24	0.99, 1.54	3.56	.06
ALL GASTRIC AND DUODENAL ULCER	10	10.42	0.96	0.52, 1.78	0.02	
CIRRHOSIS OF LIVER	35	26.19	1.34	0.97, 1.85	3.05	.10
CHRONIC NEPHRITIS	7	6.07	1.15	0.55, 2.41	0.14	
ALL ACCIDENTS	30	50.44	0.59	0.42, 0.84	8.72	.005
SUICIDE	13	18.19	0.71	0.42, 1.22	1.51	

1. P-values and confidence intervals based on M-H chi-squared for expecteds >5.0; otherwise based on Poisson; P-values are 2-tailed and not shown if > 0.1.

Table 14

Standardized Proportional Mortality Ratios for Selected Causes of Death in All White Men of Study Population (10 or More Years Duration of Employment)[1]

CAUSE OF DEATH	OBS	EXP	PMR	95% CI	CHI SQ	P
TOTAL DEATHS	1380					
ALL MALIGNANT NEOPLASMS	315	272.07	1.16	1.05, 1.28	8.55	.005
CANCER OF DIGESTIVE ORGANS AND PERITONEUM	128	81.41	1.57	1.33, 1.86	28.39	<.001
CANCER OF ESOPHAGUS	12	6.41	1.87	1.07, 3.26	4.90	.03
CANCER OF STOMACH	33	15.84	2.08	1.50, 2.90	18.82	<.001
CANCER OF LARGE INTESTINE	39	26.93	1.45	1.06, 1.97	5.52	.02
CANCER OF RECTUM	13	9.23	1.41	0.82, 2.41	1.55	
ALL CANCER OF LIVER - PRIMARY ONLY	9	5.98	1.51	0.79, 2.88	1.54	
CANCER OF PANCREAS	22	15.19	1.45	0.96, 2.19	3.09	.08
ALL CANCER OF LUNG - PRIMARY AND SECONDARY	76	82.05	0.93	0.75, 1.15	0.48	
CANCER OF SKIN	4	3.85	1.04	0.28, 2.66		
CANCER OF PROSTATE	28	27.02	1.04	0.72, 1.49	0.04	
CANCER OF TESTIS	0	0.68	0.00	0.00, 4.41		
CANCER OF BLADDER	11	10.17	1.08	0.60, 1.95	0.07	
CANCER OF KIDNEY	7	6.22	1.12	0.54, 2.35	0.10	
CANCER OF BRAIN AND OTHER CENTRAL NERVOUS SYSTEM	5	5.25	0.95	0.40, 2.28	0.01	
ALL LYMPHOPOIETIC CANCER	27	23.40	1.15	0.79, 1.68	0.56	
LYMPHOSARCOMA AND RETICULOSARCOMA	6	4.78	1.25	0.46, 2.73		
LEUKEMIA	12	9.78	1.23	0.70, 2.15	0.51	
CANCER OF OTHER LYMPHATIC TISSUE	6	6.39	0.94	0.42, 2.08	0.02	
ALLERGIC,ENDOCRINE,METABOLIC,NUTRITIONAL DIS	23	23.66	0.97	0.65, 1.46	0.02	
MENTAL,PSYCHONEUROTIC,AND PERSONALITY DISORDERS	7	4.93	1.42	0.57, 2.93		
ALL DISEASES OF NERVOUS SYSTEM AND SENSE ORGANS	6	9.43	0.64	0.29, 1.40	1.25	
ALL DISEASES OF CIRCULATORY SYSTEM	799	800.34	1.00	0.95, 1.04	0.01	
ARTERIOSCLEROTIC HEART DISEASE,INCLUDING CHD	585	532.49	1.10	1.03, 1.17	8.46	.005
ALL VASCULAR LESIONS OF CNS	112	124.59	0.90	0.75, 1.07	1.42	
ALL RESPIRATORY DISEASES	83	95.23	0.87	0.71, 1.07	1.70	
ALL PNEUMONIA	32	35.19	0.91	0.65, 1.28	0.30	
EMPHYSEMA	19	23.02	0.83	0.53, 1.29	0.72	
ASTHMA	3	2.87	1.04	0.22, 3.06		
ALL DISEASES OF DIGESTIVE SYSTEM	66	54.04	1.22	0.97, 1.55	2.77	.10
ALL GASTRIC AND DUODENAL ULCER	10	9.13	1.10	0.59, 2.03	0.08	
CIRRHOSIS OF LIVER	29	22.56	1.29	0.90, 1.84	1.89	
CHRONIC NEPHRITIS	5	5.23	0.96	0.40, 2.29	0.01	
ALL ACCIDENTS	27	42.42	0.64	0.44, 0.92	5.85	.02
SUICIDE	9	15.10	0.60	0.31, 1.13	2.51	

1. P-values and confidence intervals based on M-H chi-squared for expecteds >5.0; otherwise based on Poisson; P-values are 2-tailed and not shown if > 0.1.

Table 15

Standardized Proportional Mortality Ratios for Selected Causes of Death in all White Women of Study Population (5 or More Years Duration of Employment)[1]

CAUSE OF DEATH	OBS	EXP	PMR	95% CI	CHI SQ	P
TOTAL DEATHS	220					
ALL MALIGNANT NEOPLASMS	59	53.51	1.10	0.89, 1.37	0.79	
CANCER OF DIGESTIVE ORGANS AND PERITONEUM	16	15.49	1.03	0.64, 1.66	0.02	
CANCER OF ESOPHAGUS	0	0.52	0.00	0.00, 5.76		
CANCER OF STOMACH	2	1.90	1.05	0.13, 3.80		
CANCER OF LARGE INTESTINE	8	6.80	1.18	0.60, 2.32	0.22	
CANCER OF RECTUM	2	1.46	1.37	0.17, 4.95		
ALL CANCER OF LIVER - PRIMARY ONLY	0	1.42	0.00	0.00, 2.11		
CANCER OF PANCREAS	4	2.92	1.37	0.37, 3.50		
ALL CANCER OF LUNG - PRIMARY AND SECONDARY	7	6.35	1.10	0.53, 2.27	0.07	
CANCER OF SKIN	1	0.61	1.63	0.04, 9.11		
CANCER OF BREAST	13	10.45	1.24	0.74, 2.10	0.67	
CANCER OF ALL GENITAL ORGANS	9	7.49	1.20	0.63, 2.27	0.32	
CANCER OF ALL UTERUS	7	3.64	1.92	0.77, 3.97		
CANCER OF OTHER GENITAL ORGANS	2	3.79	0.53	0.06, 1.91		
CANCER OF BLADDER	1	0.83	1.21	0.03, 6.69		
CANCER OF KIDNEY	2	0.91	2.21	0.27, 7.93		
CANCER OF BRAIN AND OTHER CENTRAL NERVOUS SYSTEM	0	1.12	0.00	0.00, 2.67		
ALL LYMPHOPOIETIC CANCER	4	4.65	0.86	0.23, 2.20		
LYMPHOSARCOMA AND RETICULOSARCOMA	1	0.99	1.01	0.03, 5.61		
LEUKEMIA	0	1.63	0.00	0.00, 1.84		
CANCER OF OTHER LYMPHATIC TISSUE	3	1.57	1.91	0.39, 5.59		
ALLERGIC,ENDOCRINE,METABOLIC,NUTRITIONAL DIS	9	7.14	1.26	0.66, 2.39	0.50	
MENTAL,PSYCHONEUROTIC,AND PERSONALITY DISORDERS	1	0.69	1.44	0.04, 8.05		
ALL DISEASES OF NERVOUS SYSTEM AND SENSE ORGANS	0	1.98	0.00	0.00, 1.51		
ARTERIOSCLEROTIC HEART DISEASE,INCLUDING CHD	86	71.47	1.20	1.01, 1.43	4.50	.05
ALL VASCULAR LESIONS OF CNS	21	25.72	0.82	0.55, 1.22	1.00	
ALL RESPIRATORY DISEASES	5	10.45	0.48	0.21, 1.10	2.99	.08
ALL PNEUMONIA	2	4.90	0.41	0.05, 1.47		
EMPHYSEMA	0	1.32	0.00	0.00, 2.27		
ASTHMA	0	0.38	0.00	0.00, 7.88		
ALL DISEASES OF DIGESTIVE SYSTEM	10	8.31	1.20	0.66, 2.21	0.36	
ALL GASTRIC AND DUODENAL ULCER	0	0.81	0.00	0.00, 3.70		
CIRRHOSIS OF LIVER	7	3.10	2.26	0.91, 4.66		.078
CHRONIC NEPHRITIS	0	0.63	0.00	0.00, 4.76		
ALL ACCIDENTS	3	5.22	0.57	0.19, 1.73	0.97	

1. P-values and confidence intervals based on M-H chi-squared for expecteds >5.0; otherwise based on Poisson; P-values are 2-tailed and not shown if > 0.1

Table 16

Standardized Proportional Mortality Ratios for Selected Causes of Death in White Men by Origin of Birth

Underlying Cause of Death	U.S.			C. Europe			Canada			Italy		
All Causes	951			176			161			114		
	Obs/Exp	PMR	p[1]	Obs/Exp	PMR	p	Obs/Exp	PMR	p	Obs/Exp	PMR	
Malignant Disease												
All Cancer	223/198	1.13	.05	42/30.	1.40	.02	43/31.	1.37	.02	17/18.	.93	—
Digestive	85/56.	1.50	.001	17/10.	1.66	.03	20/9.7	2.06	<.001	7/6.1	1.15	—
Esophagus	9/4.8	1.88	—	1/.69	1.45	—	3/.73	4.13	.08	0/.39	.00	—
Stomach	16/10.	1.53	.10	6/2.3	2.58	.06	9/2.0	4.58	<.001	2/1.3	1.50	—
Colon	30/19.	1.61	.01	4/3.3	1.23	—	3/3.2	.95	—	2/2.1	.98	—
Rectum	8/6.3	1.28	—	2/1.3	1.59	—	1/1.1	.89	—	3/.74	4.06	.0
Pancreas	15/11.	1.36	—	3/1.7	1.74	—	3/1.8	1.69	—	0/1.0	.00	—
Liver	7/4.1	1.70	—	0/.79	.00	—	1/.74	1.35	—	0/.45	.00	—
Lung	60/64.	.93	—	7/7.2	.99	—	10/9.1	1.09	—	3/4.1	.74	—
Lymphopoietic	19/17.	1.10	—	3/2.6	1.16	—	3/2.7	1.10	—	0/1.6	.00	—
Non-Malignant Disease												
Digestive	54/41.	1.30	.05	6/5.9	1.01	—	7/6.1	1.14	—	4/3.6	1.13	—
Cirrh. of Liver	28/20.	1.41	.07	3/1.7	1.75	—	1/2.4	.42	—	2/.88	2.27	—
Respiratory	55/63.	.88	—	9/12.	.74	—	12/11.	1.07	—	5/8.5	.59	—
All Circ. Dis.	524/530	.99	—	110/109	1.01	—	89/94.	.95	—	73/72.	1.02	—
Artersel HD	396/363	1.09	—	77/69.	1.12	—	66/62.	1.06	—	53/44.	1.20	.0
All Dis. of Skin	1/.67	1.50	—	0/.13	.00	—	1/.12	8.44	—	0/.09	.00	—
Stroke	54/74.	.73	—	21/20.	1.06	—	14/15.	.96	—	13/14.	.96	—
Age at Death (Mean)	66.4			74.1			69.6			76.9		
Year of Death (Mean)	1970.5			1965.7			1968.2			1968.3		

1. Based on 2-tailed test of significance (Mantel-Haenszel X^2 used unless Exp. less than 5.0, then Poisson-P used).

Table 17

Standardized Proportional Mortality Ratios for Selected Causes of Death in White Men with 10 or More Years Exposure to Grinding, Comprehensively Defined[1]

CAUSE OF DEATH	OBS	EXP	PMR	95% CI	CHI SQ	P
TOTAL DEATHS	350					
ALL MALIGNANT NEOPLASMS	75	69.03	1.09	0.89, 1.33	0.65	
CANCER OF DIGESTIVE ORGANS AND PERITONEUM	40	20.42	1.96	1.46, 2.63	19.97	<.001
CANCER OF ESOPHAGUS	2	1.60	1.25	0.15, 4.51		
CANCER OF STOMACH	13	3.83	3.39	1.81, 5.80		<.001
CANCER OF LARGE INTESTINE	13	6.87	1.89	1.12, 3.21	5.59	.02
CANCER OF RECTUM	3	2.30	1.30	0.27, 3.81		
ALL CANCER OF LIVER - PRIMARY ONLY	0	1.48	0.00	0.00, 2.02		
CANCER OF PANCREAS	9	3.86	2.33	1.07, 4.42		.035
ALL CANCER OF LUNG - PRIMARY AND SECONDARY	13	20.95	0.62	0.37, 1.04	3.26	.08
CANCER OF SKIN	0	0.95	0.00	0.00, 3.15		
CANCER OF PROSTATE	8	7.00	1.14	0.58, 2.27	0.15	
CANCER OF TESTIS	0	0.17	0.00	0.00, 17.62		
CANCER OF BLADDER	3	2.61	1.15	0.24, 3.36		
CANCER OF KIDNEY	1	1.57	0.64	0.02, 3.54		
CANCER OF BRAIN AND OTHER CENTRAL NERVOUS SYSTEM	0	1.31	0.00	0.00, 2.29		
ALL LYMPHOPOIETIC CANCER	5	5.98	0.84	0.35, 1.99	0.16	
LYMPHOSARCOMA AND RETICULOSARCOMA	1	1.21	0.82	0.02, 4.59		
LEUKEMIA	4	2.49	1.60	0.44, 4.11		
CANCER OF OTHER LYMPHATIC TISSUE	0	1.65	0.00	0.00, 1.82		
ALLERGIC,ENDOCRINE,METABOLIC,NUTRITIONAL DIS.	6	6.05	0.99	0.45, 2.19	0.0	
MENTAL,PSYCHONEUROTIC,AND PERSONALITY DISORDERS	1	1.22	0.82	0.02, 4.55		
ALL DISEASES OF NERVOUS SYSTEM AND SENSE ORGANS	2	2.39	0.84	0.10, 3.02		
ALL DISEASES OF CIRCULATORY SYSTEM	200	203.37	0.98	0.90, 1.08	0.13	
ARTERIOSCLEROTIC HEART DISEASE,INCLUDING CHD	143	136.27	1.05	0.92, 1.19	0.55	
ALL VASCULAR LESIONS OF CNS	34	31.61	1.08	0.78, 1.48	0.20	
ALL RESPIRATORY DISEASES	28	24.98	1.12	0.79, 1.60	0.40	
ALL PNEUMONIA	6	9.19	0.65	0.30, 1.43	1.14	
EMPHYSEMA	10	6.09	1.64	0.89, 3.01	2.56	
ASTHMA	0	0.66	0.00	0.00, 4.54		
ALL DISEASES OF DIGESTIVE SYSTEM	18	13.41	1.34	0.86, 2.11	1.64	
ALL GASTRIC AND DUODENAL ULCER	1	2.27	0.44	0.01, 2.45		
CIRRHOSIS OF LIVER	8	5.49	1.46	0.74, 2.88	1.18	
CHRONIC NEPHRITIS	2	1.23	1.62	0.20, 5.87		
ALL ACCIDENTS	9	10.40	0.87	0.46, 1.64	0.20	
SUICIDE	3	3.66	0.82	0.17, 2.40		

1. P-values and confidence intervals based on M-H chi-squared for expecteds >5.0; otherwise based on Poisson; P-values are 2-tailed and not shown if > 0.1.

Table 18

Standardized Proportional Mortality Ratios for Selected Causes of Death in White Men with 10 or More Years Exposure in Machining, All Cutting Fluids[1]

CAUSE OF DEATH	OBS	EXP	PMR	95% CI	CHI SQ	P
TOTAL DEATHS	158					
ALL MALIGNANT NEOPLASMS	45	30.48	1.48	1.14, 1.91	8.69	.005
CANCER OF DIGESTIVE ORGANS AND PERITONEUM	18	9.37	1.92	1.24, 2.98	8.46	.005
CANCER OF ESOPHAGUS	1	0.72	1.39	0.04, 7.72		
CANCER OF STOMACH	2	1.89	1.06	0.13, 3.82		
CANCER OF LARGE INTESTINE	6	3.06	1.96	0.72, 4.27		
CANCER OF RECTUM	2	1.08	1.85	0.22, 6.69		
ALL CANCER OF LIVER - PRIMARY ONLY	2	0.70	2.85	0.35, 10.31		
CANCER OF PANCREAS	5	1.71	2.92	0.95, 6.83		.061
ALL CANCER OF LUNG - PRIMARY AND SECONDARY	9	8.91	1.01	0.54, 1.90	0.0	
CANCER OF SKIN	1	0.42	2.37	0.06, 13.23		
CANCER OF PROSTATE	4	3.16	1.26	0.34, 3.24		
CANCER OF TESTIS	0	0.08	0.00	0.00, 37.45		
CANCER OF BLADDER	3	1.18	2.54	0.52, 7.43		
CANCER OF KIDNEY	0	0.69	0.00	0.00, 4.34		
CANCER OF BRAIN AND OTHER CENTRAL NERVOUS SYSTEM	0	0.56	0.00	0.00, 5.35		
ALL LYMPHOPOIETIC CANCER	5	2.64	1.89	0.61, 4.43		
LYMPHOSARCOMA AND RETICULOSARCOMA	2	0.54	3.69	0.45, 13.37		
LEUKEMIA	1	1.12	0.89	0.02, 4.96		
CANCER OF OTHER LYMPHATIC TISSUE	2	0.70	2.84	0.35, 10.31		
ALLERGIC, ENDOCRINE, METABOLIC, NUTRITIONAL DIS.	3	2.70	1.11	0.23, 3.25		
MENTAL, PSYCHONEUROTIC, AND PERSONALITY DISORDERS	1	0.52	1.94	0.05, 10.68		
ALL DISEASES OF NERVOUS SYSTEM AND SENSE ORGANS	0	1.06	0.00	0.00, 2.83		
ALL DISEASES OF CIRCULATORY SYSTEM	91	92.66	0.98	0.86, 1.12	0.07	
ARTERIOSCLEROTIC HEART DISEASE, INCLUDING CHD	70	61.27	1.14	0.95, 1.37	2.04	
ALL VASCULAR LESIONS OF CNS	8	14.80	0.54	0.28, 1.03	3.50	.07
ALL RESPIRATORY DISEASES	6	10.87	0.55	0.26, 1.18	2.36	
ALL PNEUMONIA	3	4.11	0.73	0.15, 2.13		
EMPHYSEMA	0	2.64	0.00	0.00, 1.13		
ASTHMA	0	0.37	0.00	0.00, 8.10		
ALL DISEASES OF DIGESTIVE SYSTEM	6	6.06	0.99	0.45, 2.17	0.0	
ALL GASTRIC AND DUODENAL ULCER	2	1.11	1.80	0.22, 6.50		
CIRRHOSIS OF LIVER	1	2.37	0.42	0.01, 2.34		
CHRONIC NEPHRITIS	1	0.62	1.60	0.04, 8.96		
ALL ACCIDENTS	2	4.70	0.43	0.05, 1.54		
SUICIDE	1	1.66	0.60	0.02, 3.35		

1. P-values and confidence intervals based on M-H chi-squared for expecteds >5.0; otherwise based on Poisson; P-values are 2-tailed and not shown if > 0.1.

Table 19

Standardized Proportional Mortality Ratios for Selected Causes of Death in White Men with Exposure to Cutting Fluids in Machining Jobs[1]

Underlying Cause of Death	Machining All Cutting Fluids 40-111 Mo.			Machining All Cutting Fluids 120+ Mo.			Water-Based Cutting Fluids 120+ Mo.			Mineral Oil Cutting Fluids 120+ Mo.		
All Causes	111			158			20			64		
	Obs/Exp	PMR	p[2]	Obs/Exp	PMR	p	Obs/Exp	PMR	p	Obs/Exp	PMR	p
Malignant Diseases												
All Cancer	24/23.	1.04	—	45/30.	1.48	.005	9/4.8	1.89	.10	17/11.	1.52	.06
Digestive	12/6.6	1.83	.05	18/9.4	1.92	.005	3/1.3	2.38	—	8/3.8	2.09	.08
Esophagus	1/.55	1.83	—	1/.72	1.39	—	1/.11	9.23	—	0/.27	.00	—
Stomach	3/1.2	2.53	—	2/1.9	1.06	—	0/.19	.00	—	1/.90	1.11	—
Colon	4/2.2	1.82	—	6/3.1	1.96	—	1/.47	2.13	—	2/1.2	1.72	—
Rectum	1/.72	1.38	—	2/1.1	1.85	—	0/.12	.00	—	1/.48	2.11	—
Pancreas	2/1.3	1.56	—	5/1.7	2.92	.06	1/.25	3.99	—	3/.64	4.67	.06
Liver	0/.47	.00	—	2/.70	2.85	—	0/.09	.00	—	1/.30	3.29	—
Lung	7/7.5	.94	—	9/8.9	1.01	—	4/1.7	2.39	—	2/2.8	.73	—
Lymphopoietic	2/2.0	.99	—	5/2.6	1.89	—	0/.39	.00	—	4/.98	4.09	.04
Non-Malignant												
Digestive	9/4.6	1.94	.09	6/6.1	.99	—	0/.71	.00	—	1/2.4	.41	—
Cirrh. of Liver	6/2.1	2.82	.04	1/2.4	.42	—	0/.31	.00	—	0/.82	.00	—
Respiratory	7/7.6	.92	—	6/11.	.55	—	2/1.6	1.23	—	1/4.0	.25	—
All Circ. Disease	61/62.	.98	—	91/93.	.98	—	8/11.	.74	—	40/39.	1.03	—
Arterioscl. HD	50/43.	1.16	—	70/61.	1.14	—	7/7.8	.96	—	30/25.	1.21	—
All Dis. of Skin	0/.08	.00	—	0/.11	.00	—	0/.02	.00	—	0/.04	.00	—
Stroke	5/8.9	.56	—	8/15.	.54	—	1/1.5	.68	—	4/6.7	.59	—
Age at Death (Mean)	67.4			70.4			70.6			71.1		
Year of Death (Mean)	1971.0			1968.9			1978.5			1964.3		

1. Cumulative exposure duration has been weighted according to interval prior to death; see Methods, page 10.

2. Based on 2-tailed test of significance (Mantel-Haenszel X^2 used unless Exp. less than 5.0, then Poisson-P used).

Table 20

Standardized Proportional Mortality Ratios for Selected Causes of Death in White Men with Exposure to Cutting Fluids in Grinding Jobs[1]

Underlying Cause of Death	Grinding Comprehensive Definition 40-119 Mo.			Grinding Comprehensive Definition 120+ Mo.			Grinding Restrictive Definition 40-119 Mo.			Grinding Restrictive Definition 120+		
All Causes	210			350			130			193		
	Obs/Exp	PMR	p[1]	Obs/Exp	PMR	p	Obs/Exp	PMR	p	Obs/Exp	PMR	p
Malignant Diseases												
All Cancer	42/41.	1.03	—	75/69.	1.09	—	20/27.	.74	—	46/39.	1.19	—
Digestive	11/12.	.92	—	40/20.	1.96	.001	7/7.6	.92	—	24/11.	2.11	.001
Esophagus	2/.95	2.1	—	2/1.6	1.25	—	0/.64	.00	—	0/.89	.00	—
Stomach	2/2.3	.86	—	13/3.8	3.39	.001	2/1.4	1.48	—	8/2.1	3.76	.003
Colon	4/3.9	1.01	—	13/6.9	1.89	.02	3/2.6	1.17	—	7/3.8	1.83	—
Rectum	1/1.4	.74	—	3/2.3	1.30	—	0/.83	.00	—	3/1.3	2.33	—
Pancreas	1/2.3	.44	—	9/3.9	2.33	.04	1/1.5	.67	—	6/2.2	2.78	.05
Liver	1/.88	1.13	—	0/1.5	.00	—	1/.55	1.83	—	0/.84	.00	—
Lung	12/12.	.97	—	13/21.	.62	—	8/8.8	.90	—	7/12.	.59	—
Lymphopoietic	4/3.7	1.08	—	5/6.0	.84	—	0/2.4	.00	—	4/3.4	1.19	—
Non-malignant												
Digestive	16/8.9	1.79	.02	18/13.	1.34	—	12/5.8	2.07	.01	10/7.4	1.34	—
Cirrh. of Liver	8/4.0	1.99	—	8/5.5	1.46	—	6/2.8	2.13	—	6/3.1	1.96	—
Respiratory	10/14.	.71	—	28/25.	1.12	—	11/8.8	1.26	—	14/14.	1.01	—
All Circ. Dis.	111/119	.94	—	200/203	.98	—	70/71.	.98	—	105/112	.94	—
Arteriosel. HD	82/80.	1.03	—	143/136	1.05	—	54/49.	1.10	—	72/75.	.96	—
All Dis. of Skin	1/.16	6.34	—	1/.26	3.84	—	1/.10	10.4	—	1/.14	7.00	—
Stroke	13/18.	.73	—	34/32.	1.08	—	10/9.7	1.03	—	21/17.	1.23	—
Age at Death (Mean)	67.8			70.2			65.8			69.7		
Year of Death (Mean)	1969.6			1970.5			1971.2			1970.5		

1. Cumulative exposure duration has been weighted according to interval prior to death; see Methods, page 10.

2. Based on 2-tailed test of significance (Mantel-Haenszel X^2 used unless Exp. less than 5.0, then Poisson-P used).

Table 21

Standardized Proportional Mortality Ratios for Selected Causes of Death in White Men with Exposure to Oil- or Water-based Cutting Fluids in Grinding Jobs[1]

Underlying Cause of Death	Grinding Water-Based Cutting Fluids 120+ Mo.			Grinding Water/Oil Cutting Fluids 120+ Mo.		
All Causes	70			105		
	Obs/Exp	PMR	p[1]	Obs/Exp	PMR	p
Malignant Diseases						
All Cancer	17/15.	1.17	—	24/20.	1.19	—
Digestive	9/4.2	2.15	.06	14/6.2	2.28	.002
Esophagus	0/.34	.00	—	0/.47	.00	—
Stomach	3/.75	4.00	.08	5/1.2	4.15	.02
Colon	2/1.4	1.42	—	4/2.0	1.98	—
Rectum	2/.46	4.35	—	1/.71	1.40	—
Pancreas	2/.80	2.49	—	4/1.1	3.50	.06
Liver	0/.31	.00	—	0/.46	.00	—
Lung	3/4.7	.64	—	3/5.9	.51	—
Lymphopoietic	1/1.3	.79	—	0/1.8	.00	—
Non-Malignant Disease						
Digestive	1/2.8	.35	—	9/4.0	2.27	.04
Cirrh. of Liver	1/1.2	.81	—	5/1.5	3.26	.04
Respiratory	4/5.0	.80	—	10/7.4	1.36	—
All Circ. Disease	41/40.	1.04	—	52/62.	.84	—
Arteriosel. HD	31/27.	1.15	—	35/41.	.85	—
All Dis. of Skin	0/.05	.00	—	1/.08	13.2	--
Stroke	4/5.6	.72	—	13/9.9	1.31	--
Age at Death (Mean)	68.3			70.5		
Year of Death (Mean)	1971.6			1969.1		

1. Cumulative exposure duration has been weighted according to interval prior to death; see Methods, page 10.

2. Based on 2-tailed test of significance (Mantel-Haenszel X^2 used unless Exp. less than 5.0, then Poisson-P used).

Table 22

Standardized Proportional Mortality Ratios for Selected Causes of Death in White Men with Exposures in the Skilled Trades and in Forge/Heat Treat[1]

Underlying Cause of Death	Machinists 120+ Mo.			Tool and Die 120+ Mo.			Tool Grinder 120+ Mo.			Forge/Heat Treat 120+ Mo.		
All Causes	48			81			52			131		
	Obs/Exp	PMR	p[2]	Obs/Exp	PMR	p	Obs/Exp	PMR	p	Obs/Exp	PMR	p
Malignant Disease												
All Cancer	8/9.4	.85	—	16/15.	1.05	—	14/9.8	1.43	—	35/25.	1.39	.05
Digestive	7/2.7	2.58	.04	6/4.8	1.25	—	5/3.0	1.68	—	11/8.0	1.37	—
Esophagus	0/.21	.00	—	2/.35	5.65	.10	0/.22	.00	—	2/.60	3.33	—
Stomach	1/.47	2.14	—	1/1.0	1.00	—	3/.58	5.14	.04	3/1.7	1.78	—
Colon	2/.97	2.05	—	0/1.6	.00	—	1/1.0	1.00	—	2/2.6	.78	—
Rectum	0/.29	.00	—	0/.56	.00	—	0/.34	.00	—	3/.94	3.18	—
Pancreas	2/.52	3.86	—	1/.86	1.16	—	1/.55	1.82	—	0/1.4	.00	—
Liver	2/.18	11.00	.03	2/.36	5.52	—	0/.21	.00	—	1/.62	1.61	—
Lung	1/2.9	.35	—	3/4.2	.71	—	3/2.8	1.08	—	11/7.2	1.54	—
Lymphopoietic	0/.81	.00	—	5/1.3	3.87	.02	4/.84	4.75	.02	0/2.1	.00	—
Non-Malignant Disease												
Digestive	4/1.6	2.47	—	5/2.9	1.74	—	3/1.9	1.61	—	7/4.9	1.42	—
Cirrh. of Liver	3/.59	5.05	.04	1/.99	1.01	—	0/.69	.00	—	4/1.8	2.18	—
Respiratory	5/3.8	1.32	—	4/5.6	.69	—	3/3.8	.80	—	9/8.8	1.02	—
All Circ. Disease	28/28.	.99	—	49/49.	1.01	—	29/31.	.94	—	69/78.	.89	—
Arterioscl. HD	21/18.	1.12	—	34/31.	1.08	—	23/20.	1.13	—	54/51.	1.06	—
All Dis. of Skin	0/.04	.00	—	0/.06	.00	—	0/.04	.00	—	0/.09	.00	—
Stroke	6/4.7	1.28	—	5/8.1	.62	—	4/5.1	.78	—	9/13.	.72	—
Age at Death (Mean)	74.3			72.5			71.7			70.5		
Year of Death (Mean)	1973.0			1968.5			1969.2			1966.9		

1. Cumulative exposure duration has been weighted according to interval prior to death; see Methods, page 10.

2. Based on 2-tailed test of significance (Mantel-Haenszel X^2 used unless Exp. less than 5.0, then Poisson-P used).

Table 23

Standardized Proportional Mortality Ratios for Selected Causes of Death in White Men and White Women with 10 or More Years in Assembly, Packing and Related Activities[1]

Underlying Cause of Death	White Men			White Women		
All Causes	126			128		
	Obs/Exp	PMR	p[2]	Obs/Exp	PMR	p
Malignant Diseases						
All Cancer	31/25.	1.23	—	36/30.	1.19	—
Digestive	13/7.4	1.88	.02	11/9.1	1.21	—
Esophagus	1/.59	1.68	—	0/.31	.00	—
Stomach	5/1.4	3.50	.03	1/1.1	.92	—
Colon	6/2.5	2.44	.08	6/4.0	1.49	—
Rectum	2/.84	2.37	—	1/.83	1.21	—
Pancreas	0/1.4	.00	—	3/1.8	1.71	—
Liver	0/.55	.00	—	0/.83	.00	—
Lung	9/7.7	1.17	—	4/3.7	1.07	—
Lymphopoietic	1/2.2	.46	—	3/2.7	1.10	—
Non-Malignant Disease						
Digestive	9/5.0	1.80	.08	4/4.6	.87	—
Cirrh. of Liver	5/2.2	2.33	—	4/1.5	2.59	—
Respiratory	5/8.8	.57	—	3/6.3	.48	—
All Circ. Disease	68/73.	.94	—	72/72.	1.01	—
Arteriosel. HD	51/49.	1.05	—	53/43.	1.24	.08
All Dis. of Skin	1/.09	10.8	—	0/.17	.00	—
Stroke	8/11.	.74	—	11/15.	.73	—
Age at Death (Mean)	69.1			71.5		
Year of Death (Mean)	1969.7			1974.7		

1. Cumulative exposure duration has been weighted according to interval prior to death; see Methods, page 10.

2. Based on 2-tailed test of significance (Mantel-Haenszel X^2 used unless Exp. less than 5.0, then Poisson-P used).

Table 24

SPMRs for Gastrointestinal Diseases in Selected Exposure Categories for Durations of 10 or More Years[1]

		Malignant Disease					Non-Malignant Disease	
In White Men	n	All G.I.	Stomach	Colon	Pancreas	Liver	All Digestive	Cirrhosis of Liver
				SPMR				
Machining								
All CF	158	1.92	(1.06)[2]	1.96	2.92	(2.85)	0.99	(0.42)
Oil CF	64	2.09	(1.11)	(1.72)	4.67	(3.29)	(0.41)	(0.0)
Water CF	20	(2.38)	(0.0)	(2.13)	(3.99)	(0.0)	(0.0)	(0.0)
Grinding								
Comprehensive	350	1.96	3.39	1.89	2.33	(0.0)	1.34	1.46
Restrictive	193	2.11	3.76	1.83	2.78	(0.0)	1.34	1.96
Water/Oil CF	105	2.28	4.15	1.98	3.50	(0.0)	2.27	3.26
Water CF	70	2.15	4.00	(1.42)	(2.49)	(0.0)	(0.35)	(0.81)
Machinists	48	2.58	(2.14)	(2.05)	(3.86)	(11.0)	2.47	5.05
Tool and Die	81	1.25	(1.00)	(0.0)	(1.16)	(5.52)	1.74	(1.01)
Tool Grinders	52	1.68	5.14	(1.00)	(1.82)	(0.0)	1.61	(0.0)
Forge & HT	131	1.37	1.78	(0.78)	(0.0)	(1.61)	1.42	2.18
Assembly, Pkg.	126	1.88	3.50	2.44	(0.0)	(0.0)	1.80	2.33
All Categories	1532	1.52	1.97	1.39	1.43	1.35	1.24	1.34
In White Women								
Assembly, Pkg.	128	1.21	(.92)	1.49	1.71	(0.0)	0.87	2.59
All Other Categories	92	0.78	(1.23)	(0.72)	(0.86)	(0.0)	1.61	1.93

1. Cumulative exposure duration has been weighted according to interval prior to death; see Methods.

2. Based on fewer than 3 cases observed: in parentheses.

Table 25

Crude Mortality Odds Ratios for Association of Stomach Cancer with Exposures for 5 or 10 or More Years Duration[1]

	5 or More Years Exposed				10 or More Years Exposed			
	Case	Control	OR	p(2)	Case	Control	OR	p
Machining								
All CF	3	165	.57	—	2	118	.53	—
Comparison Exposure	11	346	(1.0)		11	346	(1.0)	
Grinding								
Comprehensive	14	353	1.80	.12	13	248	2.37	.03
Restrictive	9	198	2.06	.09	8	135	2.68	.04
Water/Oil CF	6	111	2.45	.08	5	69	3.28	.04
Water CF	3	77	1.76	—	3	50	2.72	.14
Tool Grinding	3	49	2.77	.13	3	37	3.67	.08
Comparison Exposure	10	453	(1.0)		10	453	(1.0)	

1. Cumulative exposure duration has been weighted according to interval prior to death; Controls exclude specific causes also associated with the exposure; Comparison Exposures exclude exposures also associated with cause of death of interest; see Methods.

2. Fisher Exact Probability.

Table 26

Distribution of Potential Confounding Risk Factors For Association of Stomach Cancer with Exposures of 10 or More Years[1]

Exposure Group		Age At Death				Year of Death				Location of Birth[2]			
	Total	30-54	55-64	65-74	75+	50-59	60-69	70-79	80+	U.S.	C. Eur.	Can.	Other
Grinding, Comprehensive	n 261	17	62	88	94	23	91	115	32	149	30	42	38
	% 100	6.5	23.8	33.7	36.0	8.8	34.9	44.1	12.3	57.5	11.6	16.2	14.6
Tool Grinding	n 40	2	10	12	16	7	13	20		29	2	5	4
	% 100	5.0	25.0	30.0	40.0	17.5	32.5	50.0		72.5	5.0	12.5	10.
Comparison	n 463	40	83	153	187	97	164	171	31	259	67	40	94
	% 100	8.6	17.9	33.0	40.4	21.0	35.4	36.9	6.7	56.3	14.6	8.7	20.3

1. For same deaths included in case-control analyses (Table 25).

2. 5 cases missing location of birth information.

Table 27

Crude Mortality Odds Ratios for Association of Colon Cancer with Exposures for 5 or 10 or More Years Duration[1]

	5 or More Years Exposed				10 or More Years Exposed			
	Case	Control	OR	p[(2)]	Case	Control	OR	p
Machining								
All CF	9	177	1.34	—	6	125	1.27	—
Oil CF	5	117	1.13	—	2	53	1.00	—
Water CF	3	39	2.03	—	1	13	2.03	—
Comparison Exposure	14	370	(1.0)		14	370	(1.0)	
Grinding								
Comprehensive	15	386	1.06	—	13	277	1.28	—
Restrictive	9	219	1.12	—	7	150	1.27	—
Comparison Exposure	18	491	(1.0)		18	491	(1.0)	

1. Cumulative exposure duration has been weighted according to interval prior to death; Controls exclude specific causes also associated with the exposure; Comparison Exposures exclude exposures also associated with cause of death of interest; see Methods.

2. Fisher Exact Probability.

Table 28

Crude Mortality Odds Ratios for Association of Cancer of Pancreas with Exposures for 5 or 10 or More Years Duration[1]

	5 or More Years Exposed				10 or More Years Exposed			
	Case	Control	OR	p(2)	Case	Control	OR	p
Machining								
All CF	5	178	2.58	.14	5	124	3.71	.05
Oil CF	4	117	3.15	.11	3	52	5.31	.05
Water CF	2	37	4.97	.10	1	11	8.36	.15
Comparison Exposure	4	368	(1.0)		4	368	(1.0)	
Grinding								
Comprehensive	9	382	1.02	—	9	267	1.46	—
Restrictive	7	214	1.42	—	6	146	1.78	.20
Water/Oil CF	4	122	1.42	—	4	78	2.22	.16
Water CF	2	83	1.04	—	2	52	1.66	—
Comparison Exposure[3]	11	476	(1.0)		11	476	(1.0)	

1. Cumulative exposure duration has been weighted according to interval prior to death; Controls exclude specific causes also associated with the exposure; Comparison Exposures exclude exposures also associated with cause of death of interest; see Methods.

2. Fisher Exact Probability.

3. This comparison group includes Machining jobs; see Table 6.

Table 29

Distribution of Potential Confounding Risk Factors for Association of Cancer of Pancreas with Exposures of 10 or More Years[1]

Exposure Group		Age At Death				Year of Death				Location of Birth[2]			
	Total	30-54	55-64	65-74	75+	50-59	60-69	70-79	80+	U.S.	C. Eur.	Can.	Other
Machining, All CF	n 129	10	23	48	48	24	24	51	12	71	26	18	13
	% 100	7.8	17.8	37.2	37.2	18.6	32.6	39.5	9.3	55.5	20.3	14.1	10.1
Machining, Oil CF	n 55	4	8	19	24	21	19	12	3	30	11	7	7
	% 100	7.3	14.5	34.5	43.6	38.2	34.5	21.8	5.5	54.5	20.0	12.7	12.7
Comparison	n 372	25	59	130	158	74	136	128	34	196	52	34	89
	% 100	6.7	15.9	34.9	42.5	19.9	36.6	34.4	9.1	52.8	14.0	9.2	23.9
Grinding, Restrictive	n 152	7	43	55	47	11	49	76	16	94	20	21	16
	% 100	4.6	28.3	36.2	30.9	7.2	32.2	50.0	10.5	62.3	13.2	13.9	10.5
Grinding, Water/Oil CF	n 82	4	19	31	28	6	36	37	3	48	11	11	12
	% 100	4.9	23.2	37.8	34.1	7.3	43.9	45.1	3.7	58.5	13.4	13.4	14.6
Comparison	n 487	42	88	161	196	99	173	181	34	274	69	43	98
	% 100	8.6	18.1	33.1	40.2	20.3	35.5	37.2	7.0	56.6	14.3	8.9	20.1

1. For same deaths included in case-control analyses (Table 28).

2. 5 cases missing location of birth information.

Table 30

Crude Mortality Odds Ratios for Association of Cirrhosis of Liver with Exposures for 5 or 10 or More Years Duration[1]

	5 or More Years Exposed				10 or More Years Exposed			
	Case	Control	OR	p[2]	Case	Control	OR	p
Machinists	3	60	1.65	—	3	31	3.20	—
Comparison Exposure	32	1058	(1.0)		32	1058	(1.0)	
Forge and Heat Treat[3]	4	176	1.11	—	4	129	1.51	
Comparison Exposure	6	292	(1.0)		6	292	(1.0)	
Grinding								
Comprehensive	12	352	1.53		8	247	1.46	—
Restrictive	8	199	1.81	—	6	136	1.99	--
Water/Oil CF	6	111	2.43	—	5	69	3.26	.04
Water CF	3	78	1.73	—	1	51	0.88	—
Comparison Exposure	10	450	(1.0)		10	450	(1.0)	

1. Cumulative exposure duration has been weighted according to interval prior to death; Other Causes of Death exclude specific causes also associated with the exposure; Comparison Expsoures exclude exposures also associated with cause of death of interest; see Methods.

2. Fisher Exact Probability.

3. Forge and Heat Treat in this analysis includes Tool Grinders, who may also have performed heat treatment of tools.

Table 31

Standardized Mortality Odds Ratios from Logistic Regression Model of Association between Stomach Cancer and Grinding Exposures in White Men[1]

n=1532 df=3

Predictors/ Risk Factors	Estimated Effect Coefficient, SE	Removal from Model[2] Δ(-2lnL)	p_1	p_2	Adjusted Odds Ratio
(Constant)	.256, .240	—	—	—	1.29
Expected Cause of Death Odds[3] (age, year adjustment)	1.00, —	—	—	—	—
Birth: Canada	.940, .424	4.72	.015	—	2.56
Grinding, Comprehensive (duration in months)	.00270, .00130	3.91	.024	—	2.25 (25 yrs. exposure)
Tool Grinding (duration in months)	.00406, .00327	1.65	.10	.20	3.38 (25 yrs. exposure)

1. Final model of log (odds) of having died from stomach cancer:

$$\ln\left(\frac{p}{1-p}\right) = .256 + 1.00 \ln\left(\frac{r_i}{1-r_i}\right) + .940 I_B + .00270 X_G + .00406 X_T$$

where:

r_i is age-, year-, sex-, race- specific proportional mortality rate for stomach cancer in U.S. population in 5-yr. intervals; $\ln\left(\frac{r_i}{1-r_i}\right)$ is log (odds);

I_B is indicator of Canadian birth (1 = Canada, 0 = not);

X_G is weighted duration of exposure in Grinding, Comprehensive in months (see Methods);

X_T is weighted duration of exposure in Tool Grinding in months.

2. Change in - 2log(likelihood) for removal of single risk factor from final model, one at a time, and associated P-value: 1-tailed (p_1) for hypothesized effects, 2-tailed (p_2) for others.

3. Effect estimate fixed at 1.0 in estimation procedure.

Table 32

Standardized Motality Odds Ratios from Logistic Regression Model of Association Between Cancer of the Pancreas and Grinding and Machining Exposures in White Men[1]

n=1532 df=4

Predictors/ Risk Factors	Estimated Effect Coefficient, SE	Removal from Model[2] Δ(-2lnL)	p_1	p_2	Adjusted Odds Ratio
(Constant)	-.066, .32	—	—	—	0.93
Expected Cause of Death Odds[3] (age, year adjustment)	1.00, —	—	—	—	—
Machining, Oil CF (duration in months)	.00765, .00266	5.98	.007	.014	9.9 (25 yrs. Exposure)
Grinding, Comprehensive, (durations in months)	.00050, .00224				4.8 (25 yrs. Exposure and DOH = 1918)
Date of Hire (Months after 4/1933)	.00235, .00322	10.5	.009	.018	
Grinding - Date of Hire Interaction	-.000034, .000014				1.16 (25 yrs. Exposure and DOH = 1933)

1. Final model of log (odds) of having died from cancer of pancreas:

$$\ln\left(\frac{p}{1-p}\right) = -.066 + 1.00 \ln\left(\frac{r_i}{1-r_i}\right) + .00765X_M + .0005X_G + .00235\text{DOH} - .000034\text{ITR}$$

where:

r_i is age-, year-, sex-, race-specific proportional mortality rate for cancer of pancreas in U.S. population in 5-yr. intervals; $\ln\left(\frac{r_i}{1-r_i}\right)$ is log (odds);

X_M is weighted duration of exposure in Machining, Oil cutting fluids, in months (see Methods);

X_G is weighted duration of exposure in Grinding, Comprehensive definition, in months;

DOH is date of hire, in months later than April, 1933 (approximate population mean date of hire);

ITR is date of hire, Grinding (Comprehensive) interaction (DOH x X_G) in (months).

2. Change in - 2log(likelihood) for removal of single risk factor or group of risk factors from final model, one at a time, and associated P-value: 1-tailed, (p_1) for hypothesized effects, 2-tailed (p_2) for others.

3. Effect estimate fixed at 1.0 in estimation procedure.

Table 33

Standardized Mortality Odds Ratios from Logistic Regression Model of Association between Lung Cancer and Forge, Heat Treat Exposures in White Men[1]

n=1532 df=1

Predictors/ Risk Factors	Estimated Effect Coefficient, SE	Removal from Model[2] $\Delta(-2\ln L)$	p_1	p_2	Adjusted Odds Ratio
(Constant)	-.167, .124	—	—	—	0.85
Expected Cause of Death Odds[3] (age, year adjustment)	1.00, —	—	—	—	—
Forge, Heat Treat (duration in months)	.00230, .00120	3.29	.035	.070	1.99 (25 yrs. exposure)

1. Final model of log (odds) of having died from lung cancer:

$$\ln\left(\frac{p}{1-p}\right) = -.167 + 1.00\ln\left(\frac{r_i}{1-r_i}\right) + .00230X_F$$

where:

r_1 is age-, year-, sex-, race-specific proportional mortality rate for lung cancer in U.S. population in 5-yr. intervals; $\ln\left(\frac{r_i}{1-r_i}\right)$ is log (odds);

X_F is weighted duration of exposure in Forge, Heat Treat, Heading and Annealing (see Methods).

2. Change in - 2log(likelihood) for removal of single risk factor from final model, one at a time, and associated P-value: 1-tailed (p_1) for hypothesized effects 2-tailed (p_2) for others.

3. Effect estimate fixed at 1.0 in estimation procedure.

Table 34

Standardized Mortality Odds Ratios from Logistic Regression Model of Association Between Cirrhosis of Liver and Grinding and Machinist Exposures in White Men[1]

n=1532 df=2

Predictors/ Risk Factors	Estimated Effect Coefficient, SE	Removal from Model[2] $\Delta(-2\ln L)$	p_1	p_2	Adjusted Odds Ratio
(Constant)	.147, .201	—	—	—	1.16
Predicted Cause of Death Odds[3] (age, year adjustment)	1.00, —	—	—	—	—
Machinist	.00602, .00265	3.42	.03	.07	6.08 (25 years exposure)
Grinding, Water/Oil CF	.00340, .00267	1.96	.08	.16	2.77 (25 years exposure)

1. Final model of log (odds) of having died from cirrhosis of liver:

$$\ln\left(\frac{p}{1-p}\right) = .147 + 1.00\ln\left(\frac{r_i}{1-r_i}\right) + .00602X_M + .00340X_G$$

where:

r_1 is age-, year-, sex-, race-specific proportional mortality rate for cirrhosis of liver in U.S. population; in 5-yr. intervals; $\ln\left(\frac{r_i}{1-r_i}\right)$ is log (odds);

X_M is weighted duration of exposure in Machinist (skilled trade), in months (see Methods);

X_G is weighted duration of exposure in Grinding, in Water/Oil, in months.

2. Change in - 2log(likelihood) for removal of a single risk factor from final model, one at a time, and associated P-value: 1-tailed, (p_1) for hypothesized effects, 2-tailed (p_2) for others.

3. Effect estimate fixed at 1.0 in estimation procedure.

Table 35

Goodness of Fit of Logistic Regression Models for Key Associations

Outcome	Exposure	Exposure Strata (Mo.)					Total
		0	1-50	51-150	151-350	351+	
Stomach Cancer	Grinding, Comprehensive						
Total No. in Stratum		883	121	232	243	53	1532
No. of Cases Predicted[1]		16.96	2.09	4.94	8.39	2.60	34.99
No. of Cases Observed		17	3	5	8	2	35
Cancer of Pancreas	Machining, Oil CF						
Total No. in Stratum		1336	29	118	44	5	1532
No. of Cases Predicted[1]		18.7	.54	2.52	1.91	.74	24.41[2]
No. of Cases Observed		18	1	3	1	1	24
Cancer of Pancreas	Grinding, Comprehensive						
Total No. in Stratum		883	121	232	243	53	1532
No. of Cases Predicted[1]		12.42	1.72	2.81	4.37	3.10	24.42[2]
No. of Cases Observed		13	2	1	5	3	24
Cancer of Lung	Forge, Heat Treat						
Total No. in Stratum		1312	28	76	99	17	1532
No. of Cases Predicted[1]		65.7	1.91	5.34	7.82	2.20	82.99
No. of Cases Observed		64	2	8	7	2	83

1. No. Predicted = $\sum_{s} (1 + e^{-(A_0 + \ln(\frac{r_i}{1-r_i}) + B_1X_1 + B_2X_2 \ldots)})^{-1}$; s: over stratum

(See Tables 31-33 for coefficients A_0, B_i)

2. Regression estimates used were approximate because they are averages over successive interations of oscillating final convergence, causing sum of predicted to differ from sum of observed.

APPENDIX

MODELLING PROPORTIONAL MORTALITY

USING LOGISTIC REGRESSION

Traditional Analysis of Proportional Mortality

Analysis of mortality patterns in a study population that consists of all deaths occurring for some specified cohort (over some time interval) has traditionally been accomplished either with 1) external standardization for age at death, year of death, sex and race, using some reference population, as in standardized proportional mortality ratio (SPMR) analysis[1] or 2) internal standardization either by stratification on confounding covariates, where feasible, as in case-control analysis of proportional mortality (i.e. conditional on the death of study population members),[2] or by estimation of covariate effects using logistic regression in case-control analysis.

The limitations inherent in SPMR studies include the inability to directly assess exposure and confounding except by defining distinct subpopulations of presumed equivalent exposure and covariate status. Besides the loss of power with diminishing population size, there is the problem of non-comparability of SPMR estimates across populations of different age, year of death, etc. The description of exposure effects in relation to duration and latency (remoteness of exposure experience in time) is similarly inhibited in SPMR analysis. Another limitation is that of selection effects operating on the cohort that result in its not being a stratified random sample of the reference population (i.e. stratified on age at death, year, etc.). This selection arises in three primary ways in occupational disease studies: 1) selection for healthy individuals at hiring, 2) selection for sustained good health in populations specified as having some minimal duration of employment, and 3) the specific ethnic compositions of industrial workforces, aside from race (for which reference population data is specific). These selection effects have to be considered in the interpretation of SPMR results.

Case-control analysis largely avoids the problem of selection effects on the cohort except to the extent that selection is associated with departments, job classifications or exposures. (Early attrition from an industrial population due to adverse health effects of exposures is a general source of bias for all types of analysis, tending to cause underestimation of exposure effects.) However, case-control analysis based on discrete risk factors (contingency tables) suffers the same loss of power with increasing stratification into subpopulations of equivalent exposure and other risk factors as SPMR analysis, and case-control analysis using regression methods must expend substantial statistical resources in estimating the usual covariate effects (age, year of death, etc.) that are freely available in an external standardization (SPMR).

In studies where the excess number of observed cases, over expected, is barely statistically significant, a more efficient analysis than traditional SPMR or case-control contingency tables is needed.

A Logistic Regression Model for Proportional Mortality.

An efficient model should incorporate the known dependence of proportional mortality rates on age at death, year, etc.; should allow for some deviance from these expected rates arising from a general selection effect in the cohort; and should allow estimating other simultaneous effects, both discrete (e.g. origin of birth, type of work) and continuous (e.g. cumulative measures of exposures), and possible interactions.

One approach that has been developed is to model the odds of death having occurred due to some particular underlying cause compared with all other causes by using the logistic regression method:

$$\left(\frac{p}{1-p}\right) = e^{a+b_1X_1+b_2X_2+\ldots} \quad \text{or} \quad \log\left(\frac{p}{1-p}\right) = a+b_1X_1+b_2X_2+\ldots$$

where p is the probability that a death was the result of the underlying cause specified.(3)

In order to utilize the reference population's known proportional mortality rates the expected odds, specific for age at death, year of death (in 5 yr. intervals), sex and race, are included in the model in the form

$$X_1 = \log\left(\frac{r}{1-r}\right)$$

where r is the age, year, etc., specific proportional mortality rate for the specified cause, in the reference population. The model is now:

$$\log\left(\frac{p}{1-p}\right) = a+b_1 \log\left(\frac{r}{1-r}\right) + b_2X_2 + \ldots$$

In the absence of any other effects (i.e., $b_2=b_3=\ldots=0$), we would expect a = 0 and b_1 = 1 if the study population is a stratified random sample of the reference population; otherwise, if selection is acting on the cohort, a and b will jointly reflect that selection. Ideally one would like to constrain b_1 to equal 1.0. This would result in the intercept a_0 being an estimate of the standardized mortality odds ratio (SMOR) for the entire study population relative to the reference population, adjusting for exposure and other risk factors included in the model. This can be accomplished using available statistical packages such as BMDP.(3)

Use of the expected odds of death from a particular cause, in the regression model, is an example of using a multivariate confounding score, as proposed by Miettinen,[4] but in this case based not on the observed data but on that of a reference population. A single variable is used to summarize the joint effects of age and year of death.

Risk factors or exposures that are modelled by the terms b_iX_i are presumed to modify the expected odds uniformly over the covariate strata in this model, i.e. by a fixed factor independent of age at death, year of death, etc. Inclusion of interaction terms would allow assessing covariate-risk factor interactions, such as an exposure with chronological time dependence (due to changing nature of exposure): $b_{ij}X_iX_j$, where X_i is an exposure measure, X_j a chronological time measure, appropriately offset by some mean value.

Modelling the odds of death from a specific cause provides an exact estimate of the actual cause-specific mortality rate ratio associated with an exposure in the full cohort (in the absence of selection effects), because the mortality odds ratio is identical to the mortality rate ratio[5] in a stationary population when the exposure is not associated with any other causes of death. When selection is present, the intercept estimate allows separation of that selection effect that is common to the full study population. Therefore, the resulting standardized mortality odds ratio estimate for an exposure is an estimate of the actual standardized mortality rate ratio.

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