



**MORTALITY IN WORKERS IN ELECTROMECHANICAL
AND ELECTRONICS PRODUCTION**

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**INTERNATIONAL UNION, UNITED AUTOMOBILE,
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16. Abstract (Limit: 200 words) Concern expressed by a local union over excess cancer deaths at an electronics and electromechanical manufacturing facility for aircraft and missile applications prompted this mortality study. Workers in this industry are exposed to machining and grinding operations, armature construction, and various assembly operations. Chemical exposures included halogenated solvents, cutting fluids, solder fluxes, epoxy resins, cyanoacrylate resins, and acrylonitrile based resins. From 1965 to 1979 there were 30 deaths from cancer among female workers; 15.5 was the expected number. From 1970 to 1979 there appeared to be significant excess proportions of deaths attributable to pancreatic cancer in men and women and of colon cancer, stomach cancer and ovarian cancer in women. Exposure to epoxy like materials may have some relationship to colon cancer among women and pancreatic cancer among men. Ovarian cancer appeared to be linked with inspection and possibly ~~electromechanical assembly operations~~. From 1980 through 1983, there has been no evidence of increased cancer; however, the numbers are small. The authors recommend that an independent hygiene assessment be made of current production, paying strict attention to ventilation systems, resin handling systems, solvent use, and cutting fluid control in the grinding and machining operations. The establishment of a hazardous materials control committee is recommended.			
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PREFACE

This is the fifth in a series of six mortality reports conducted under the terms of NIOSH Contract No. 210-81-5104.

The original concern and investigative work which led to this study came from Terry Entrican who, at that time, was the health and safety representative of Local 330, Grand Rapids, Michigan. Dr. Barbara Silverstein of the University of Michigan assisted in generating the materials needed for characterizing exposure history at this plant.

We are particularly thankful for the indispensable and considerable clerical and secretarial efforts contributed by Carole Rogers, Margaret Auch, Pamela Poe, and Melanie Bogoevich.

The Lear Siegler Company, Instrument Division, cooperated in providing some of the death certificates analyzed, records of industrial hygiene samples, access to the plant for two inspections, and consultation on past and current work processes and exposures. Lear Siegler received a copy of the draft report for review and comments.

Mention of company name or products does not constitute endorsement by the National Institute for Occupational Safety and Health.

MORTALITY IN WORKERS IN ELECTROMECHANICAL AND ELECTRONICS PRODUCTION

Prepared by:

**International Union, United Automobile,
Aerospace and Agricultural Implement
Workers of America (UAW)**

NIOSH CONTRACT #210-81-5104

SUMMARY

Electronics and electromechanical manufacture for aircraft and missile applications is a relatively new industry. Exposures to potentially hazardous chemicals in this industry have changed substantially over the past 50 years. Production activities have included machining and grinding, armature construction, and a variety of assembly operations. Materials have included various halogenated solvents, cutting fluids, solder fluxes, and several distinct polymer systems such as epoxy-, cyanoacrylate-, and acrylonitrile-based resins.

Local union concern over cancer deaths at one such plant led to this mortality study. A list of 31 cancer deaths compiled by the local union included 11 of the 35 cases at sites subsequently identified as having elevated proportional mortality. The study population (n=297) consisted of all deaths occurring 1958-1983 among current or former hourly employees with 10 or more years' service, whose duration of service when weighted to account for latency exceeded 4 years. Work histories were derived from seniority lists, beginning in 1952; an exposure classification was defined by broad categories of materials used and by departmental groupings.

Standardized proportional mortality ratios were computed, and statistically significant excess proportions of deaths were observed due to cancer of the pancreas in men and women (SPMR=3.1) and cancer of the colon, stomach and ovaries in women (SPMR=2.5, 4.8, and 4.1, respectively). These excesses were concentrated in the period 1970-79 and appear to be absent after 1979.

Case-control studies with both crude and standardized mortality odds ratios, adjusted for age and year of death, indicate associations of colon cancer with exposures to epoxy-like materials in women, ovarian cancer with inspection and possibly electromechanical assembly operations, and in men, pancreatic cancer with exposures to epoxy-like materials. In the case of cancer in women workers, the associations suggest that exposures occurring prior to the 1960s are responsible.

BACKGROUND

Origin of Study

The production of aircraft instruments and control systems has developed in the past 50 years. In the early decades, production involved both gross and fine machining, armature winding, other fabrication activities, and pre-semiconductor electronics assembly. In subsequent decades, production evolved to include guided missile control systems and the technology of integrated circuits and microelectronics; gyroscopic instruments have evolved to include inertial guidance systems. The exposures common in this industry have included: cutting fluids used in metal machining, usually on light-weight alloys; insulating materials in armature and coil winding and small motor production; rosin core soldering in electronic component assembly, and a variety of organic bonding and sealing agents in instrument and electromechanical device assembly. There has been solvent usage in a number of areas and widespread contact with epoxy, acrylic, cyanoacrylate and other polymer systems.

The Lear Siegler Company, Instrument and Electromechanical Divisions, located in Grand Rapids, Michigan, pioneered in the development of aircraft instruments, auto-pilots and control devices in the 1940s. In the late 1950s, the Electromechanical Division, which manufactured power actuators, was moved to Cleveland. The UAW has represented Lear Siegler workers in Grand Rapids since 1948. The number of active employees has varied between 800-2,000 over this period. Partly in response to attention given occupational cancer hazards by the International Union, the local union began to compile incident cancer cases and deaths. In 1980, a list containing 31 deaths due to cancer and 23 additional cancer diagnoses was prepared by the local union and assistance was requested because of their perception of an unusually high cancer rate in their membership. The UAW Health and Safety Department requested further information on all known deaths and then performed some preliminary analyses to assess the completeness of the list of deaths and to compute standardized proportional mortality ratios. Based on that analysis and the availability of records from the local union allowing construction of a larger study population with work histories, a full study was undertaken.

METHODS

Design

A standardized proportional mortality study was carried out for a study population of hourly employees with 10 or more years' service in an electronics plant who died between January 1, 1958 and December 31, 1983. Case-control analyses were performed using a logistic regression model of mortality odds to examine associations between particular causes of death and exposure histories. Potential confounding variables include age at death, year of death, country of birth, and sex. A standardized mortality ratio analysis (SMR) was not chosen because substantially more resources would have been needed and race was unknown for the living cohort.

Prior hypotheses were based on the known likely exposures and included: 1) the association of cancer of the gastrointestinal tract with cutting fluid exposures;^(1,2) 2) association of cancers of liver and pancreas with chlorinated hydrocarbon solvent exposures;⁽³⁻¹⁶⁾ 3) association of unspecified cancer with epoxy and other polymer resin exposures;⁽¹⁷⁻²⁶⁾ and 4) association of brain cancer with exposures in electronics or electromechanical production.⁽²⁷⁾ However, the main thrust of the analysis was exploratory hypothesis generation in this population which is somewhat unique as one of the early aerospace electronics cohorts.

Study Site

The company was located in downtown Grand Rapids from 1948 until 1959, at which time a suburban plant was built. The earlier downtown plant was a multi-story facility and included several buildings. The more recent plant is a single-story facility with large, open production areas and several enclosed, controlled environments referred to as "clean rooms" or "laboratories." The latter areas have highly filtered air circulation and operate at positive ambient pressure. During the 1950s, 90 percent of production consisted of electromechanical devices and 10 percent was electronics; by the 1980s 70 percent was electronics and 30 percent electromechanical production. Electromechanical products were gyro systems and other devices for instruments and navigation systems and a variety of power actuators for aircraft or missile control surfaces.

The production activities where potentially significant chemical exposures have been possible were primarily in fabrication and assembly. In fabrication, a variety of machining work has been done, including automatic bar machining, milling, boring, grinding and drilling. The metals machined were usually light alloys, including aluminum and titanium, but occasionally beryllium has been machined. Sheet metal operations also have been done, and injection molding of plastics was once carried out in the fabrication division. Subsequent steps in fabrication included welding (gas, arc, heli-arc), deburring, tumbling, lapping and cleaning of various parts. Some parts went through heat treat or plating processes. Because high machining tolerances were required, there was frequent cleaning with solvents and gauging of parts during machining steps, and there

were large inspection operations. The fabrication activities were consolidated in a few large areas making up several departments.

Assembly of motors and gyros required lamination of steel sheets for rotors and stators using organic bonding agents such as epoxy resins. Coils were wound from insulated wire and inserted into the laminated frames. Various bonding agents were used. Assembled laminations were ground using soluble cutting fluids. Other manufactured components include diaphragms for pressure indicators and a variety of electronic circuit boards.

Electronic assembly generally involved placement of components on circuit boards or other substrates, frequently using epoxy bonding agents, and connection of wires using a rosin core solder. While some steps of this process have been automated, allowing component insertion and wave-soldering of entire boards, much of the assembly involved detailed manual manipulation by assemblers whose work is carried out in their immediate breathing zone, often under microscopic examination. Printed circuit boards have been manufactured as well as purchased. Microelectronic production involving vacuum deposition or silk screen techniques has been carried out increasingly since the 1950s. All microprocessors used in assembly are purchased. Solvent use is widespread in electronics assembly, although the volume of solvents is not large.

Electromechanical assembly for larger devices, such as "screw jacks" or linear actuators, has involved chemical exposures primarily to lubricants and to bonding agents such as Loctite^(R) products for insuring fixed placement of mechanical components; pre-1950 production used exclusively mechanical means. Gyro systems assembly takes place in controlled environments and requires intensive solvent cleaning and the use of organic bonding agents. Instruments and self-contained navigation systems also are assembled in "clean room" environments, with laminar flow hoods (blowing into room). Exposures are primarily organic bonding agents, solvents and, minimally, soldering.

The study site was in Kent County, Michigan, a county with one of the highest proportions of Dutch ancestry in the U.S.,⁽²⁸⁾ mostly second and third generation. The possibility of confounding risk factors arising from Dutch ancestry was therefore examined.

Industrial Hygiene Measurements

Results were available from a limited number of air samples for chemical exposures taken at the study plant between 1976 and 1983 by the employer, the state department of public health, and the employer's insurance company. In most cases there was very little information on the sampling strategy, methods of sampling, and analysis or test conditions. Tests appear to have been made in response to specific complaints or concerns and do not reflect a systematic effort to determine representative environmental conditions or individual exposure profiles.

Four short-term area samples for airborne "mineral oil mist" were taken in 1976 in the automatic machining area. Results were all reported as less than 2mg/m³, but methods of sampling and analysis were not specified.

On five occasions between 1978 and 1982, air samples for airborne carbon dioxide were taken in the area of environmental test chambers which use liquid carbon dioxide to create a cold cycle for instrument testing. In general, these were short-term, direct reading breathing zone measures. Mean values for the five surveys were: 37,000 ppm (n=6 area samples), 5700 ppm (n=7), 200 ppm (n=2), 20,000 ppm (n=14), 1880 ppm (n=5).

Sampling was conducted for a variety of organic solvents. Single four- to six-hour time-weighted average exposures were recorded for methanol (1 ppm breathing zone, on wire bonding), n-hexane (2 ppm breathing zone, on wire bonding), and isopropyl alcohol (12 ppm breathing zone, on solder touch-up). Five surveys for methylene chloride were made on degreasing and wiping jobs. A total of 16 direct reading breathing zone tests were taken with a mean level of 125 ppm (SD=102). A single 6-hour time-weighted average of 14 ppm was also reported for the breathing zone on a wire bonding job. Three surveys were made for Freon 113 on machining, plating and degreasing jobs. A total of 18 breathing zone time-weighted average exposures were reported with a mean of 8.4 ppm (SD=13.9). Five surveys were made for methyl chloroform on machining, plating, degreasing and solder jobs. Thirteen samples, mostly short term breathing zone, were reported with a mean of 28 ppm (SD=29). Five surveys for perchlorethylene were made on machining, plating, degreasing and parts cleaning jobs; 29 samples, mostly short-term breathing zone, were reported with a mean of 51 ppm (SD=56).

Study Population: Definition and Identification

The study population was defined to be:

all UAW members who had been employed at the study plant for 10 or more years, who died between January 1, 1958 and December 31, 1983, and whose years of service exceeded 4 years when weighted to take account of the latency of fatal chronic diseases in relation to potential causes (see Exposure Classification, below).

The 10-year requirement in this definition was chosen in order to make use of pension records kept at the local union. Annual pension reports were available for all but two years in the period 1958-1983 and listed all current employees, those on lay-off or other leave, and all those who had left employment with 10 or more years' service, including both pensioners and deferred vested workers (having pension rights but not yet old enough to collect a pension). In addition, all deaths known for the previous year were identified. These annual reports thus largely specified the risk group of candidates for the study population.

The choice of four years for the minimum duration of employment, weighted to account for latency, was made prior to analysis and represents a balance between restriction to those at higher risk for work-related, long-latency disease, and maintaining adequate population size. In weighting for latency, consecutive time intervals were multiplied by a factor which had the value of 1.0 for times remotely in the past, prior to death, and approached

0.0 for times immediately prior to death. (A logistic weighting function was used; see Methods: Exposure Classification).

Additional candidates for the study population included the original list of deaths provided by the local union (which overlapped considerably with those identified from pension reports). All former employees who had once been assigned a sequential retirement number or deferred vesting number, but whose names and numbers no longer appeared in the latest pension report, also were considered likely candidates for the study population and their identities were sought. Altogether 723 former employees were identified as known to be, or possibly, deceased members of the cohort at risk. (Active employees and pensioners identified at the study closing date were all assumed to be alive.)

Vital status for study population candidates not known to be deceased was determined three ways:

1. computer matching to the State of Michigan death registry, using social security number and name, for deaths occurring 1970-1982;
2. computer matching to the Social Security Administration's file of known deceased (using a commercial vendor), also using social security number and name, for deaths occurring approximately 1965-1982;
3. manual matching to a microfilm death index of the State of Michigan for deaths occurring 1950-1982, using name, age and date of death, and county of death. Those matches were confirmed by inspection of death certificates using, e.g., social security number and date of birth.

A total of 414 deaths was identified, constituting the candidate study population; cause of death for 382 was obtained directly from the Michigan death registry (n=189) or from copies of death certificates (n=193). Underlying cause of death in the Michigan death registry is coded according to NCHS procedures in the International Classification of Diseases (ICD) revision current at the time of death. For all deaths for which death certificates were obtained, underlying cause together with multiple causes were coded by an NCHS nosologist in the ICD revision current at death (except that all deaths after 1978 were coded in ICD-8).

Country and date of birth, sex, race and age information as well as causes of death were coded for data entry by one person and verified by another.

Job Histories

Date of hire (and date of birth) was available from pension report listings. Date of termination was available for many in the study population from the same source.

The local union had retained seniority lists from 1952. These lists give all current employees and their seniority (hire) dates, clock numbers, job

classification and department. Seniority lists for the following years were placed in computer files and edited for matching to the study population: 1952, 1955, 1958, 1961, 1965. Matching was based on name, seniority date and clock number (when available). Matching failures (based on known employment dates) and ambiguous matches were examined for possible name changes or spelling variants. Job classification numbers identifying specific jobs have largely been consistent over the period 1952-1979, although there have been a few major redefinitions. These latter, however, occurred mostly after 1965. Department designations, on the other hand, changed with each seniority list used (at approximately three-year intervals). Employment history prior to working at Lear Siegler was unavailable for this study population.

Exposure Classification

The exposures of primary interest were grouped into five broad categories:

1. solvents (such as carbon tetrachloride, chloroform, perchloroethylene, trichloroethane, and methylene chloride);
2. epoxy resin and analogous slow-setting polymer systems (used mainly in electronic and instrument assembly);
3. cyanoacrylate and other polymer adhesives; elastomers and sealers (used mainly in instrument and electromechanical assembly);
4. solder and rosin-core flux fumes;
5. cutting fluids.

In order to construct exposure histories, job classifications were assigned an exposure profile based on the production activity comprising the job. This description was derived from: 1) a manual of job descriptions, 2) a narrative describing the overall production process prepared by a union member, 3) two walk-throughs of the plant, and 4) discussions with plant and union officials.

Each of 224 job classifications was profiled or ranked for the five exposure categories, in three possible levels: 1) little or no exposure (level=1), 2) moderate exposure relative to the highest exposures in plant (level=2), and 3) relatively high exposures (level=4). The assignment of exposure levels as 1, 2 or 4 was intended only to approximate roughly actual, relative exposure levels.

Approximately 160 departments, that existed at one time or another in the five seniority lists, were grouped according to generic activity characteristics, such as machining, instrument assembly, motor winding, etc. Table 1 shows these departmental groups. Departments and departmental groups were characterized using the same information sources used to define job classifications; however, for the years 1958 and later, when explicit department titles were not generally available, departments were further defined by the mix of job classifications occurring within them. Departments

and departmental groups were profiled on the five exposure categories the same way jobs were.

Thus, at up to five points in time (approximately every three years) for each worker, a job classification, department and departmental group were specified. Based on the exposure profile for the specific job classification and department at a point in time, a joint exposure measure was computed as the product of the job and department exposure profiles: i.e., (1, 2, or 4) x (1, 2, or 4) → (1, 2, 4, 8, or 16). This exposure measure takes both specific job classification and departmental environment into account in producing an approximate ranking of actual exposure experience; it assigns relatively high exposures only when both job classification and department are consistent with such exposures. The choice of a multiplicative joint measure was intended to generate a greater spread in the ranking of the exposures and assign high values only for those most certain to be high. (However, an additive model could also have been used, probably with minimal impact, depending on the choice of value assignments to the exposure levels of jobs and departments (e.g., 0, 1, 2 versus 0, 1, 4...)).

Cumulative durations were computed as follows. For the five exposure categories, the lengths of time spent at specific joint exposure levels were multiplied by those levels and summed together. (The joint exposure levels used were transformed from the set (1, 2, 4, 8, 16) to (0, 1, 2, 4, 8) so that "no significant exposure" had a level "0"). Time intervals spent in each departmental grouping also were summed.

In summing the contributions from different time intervals, the contributions were weighted in order to account for presumed latency of disease and death, in relation to time of exposure, as follows:

1. Roughly three-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 three-year intervals, the interval length was 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 $a = 0.4/\text{year}$ and $b = 12.5$ years, the resulting function weights exposures at times prior to death as indicated in Table 2.

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 based on prior knowledge to produce a plausible dependence for the risk of long-latency disease on previous exposure, such as for malignancies of the GI tract or lungs. This weighting function had been used in a previous study of stomach, pancreatic and lung malignancies.(2)

4. For workers whose date of hire occurred prior to the first seniority list interval (the three-year interval centered on 1952), the cumulative exposure in each exposure category or departmental group was increased by a fixed factor computed individually for each worker. The factor was the ratio of the latency-weighted cumulative time accrued while ever employed at this plant to the latency-weighted cumulative time accrued while employed in the period covered by seniority lists (three-year intervals). Every worker with job history data had a known date of hire and all were after 1941. Exposures later than 1966 were defined to be the same as those indicated by the 1965 seniority list and, in any case, contributed little to a worker's cumulative exposure (since such exposures occurred within 15 years of death).

The resulting cumulative exposure measures, for both the five broad categories and the departmental groupings, were used: 1) to define subpopulations of presumed higher exposure for SPMR analyses, and 2) as continuous exposure measures in logistic regression analyses of mortality odds.

When the latency-weighting procedure was applied to all time intervals in which a worker was employed, without regard to exposure status, a latency-weighted duration of employment resulted. This employment duration was the basis for excluding from the study population all those whose (weighted) duration of employment was less than four years. For a worker employed continuously until death, this exclusion corresponds to a minimum employment duration of approximately 16 years.

Another set of analogous exposure measures was computed when it became apparent that the observed excess proportional mortality for a subset of cancer sites was concentrated in the early 1970s, implying that the putative exposures were limited to the period prior to the 1960s. These exposure measures were constructed precisely as described above, except that the contribution from each time interval was further multiplied by a chronological weighting function which took the value 1.0 up to the mid-1950s but rapidly approached zero as chronological time proceeded into the 1960s. The function used was:

$$(1 + e^{.72(T-1959)})^{-1},$$

where T is the mid-point of an exposure interval in chronological time, in years. The values taken at the beginning of 1955, 1959, and 1963 were .946, .5, .053, respectively.

Analysis

Standardized proportional mortality analyses were performed using Monson's program⁽²⁹⁾ and reference rates for the U.S. national population, updated through 1980. Analyses were performed for major subpopulations based on exposure. Two-tailed P-values and 95 percent confidence intervals were based on the Mantel-Haenszel chi-squared statistic generated by the PMR program if the expected deaths numbered 5 or more; when less than 5 were expected, the P-value and confidence interval were two-tailed Poisson.⁽³⁰⁾

Because important confounding and multiple exposures were potentially present, logistic regression analyses of mortality odds were performed for the key associations identified in the SPMR analysis, simultaneously adjusting for age at death and year of death (see Appendix for detail on this method). The algorithm used computes an unconditional, maximum likelihood estimate, and is contained in the BMDP statistical program.⁽³¹⁾ The outcome measure (case/control) was defined with no exclusions — controls were all non-cases — and the logistic regression modeled the odds of being a case, i.e., of a death having resulted from a specified underlying cause. No exclusions from controls were made because there were no definite prior known associations of the exposures under study with other causes of death, and for simplicity in preparation of the expected odds. Although there were specific jobs with known hazards besides those of interest, no exclusions from the study population were made because: 1) the expected attributable outcome was lung cancer, an outcome not focused on in this study; 2) the jobs (welding, heat treat, plating, maintenance) were generally coded as unexposed for the exposures of interest; and 3) the numbers of workers involved were small.

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 coefficient fixed at 1.0 (using procedure BMDP3R⁽³¹⁾). Other terms included were cumulative exposures (weighted) in specific exposure categories (with no minimum durations required). The general model used was as follows (see Appendix):

$$\ln \left(\frac{p}{1-p} \right) = a_0 + 1.0 \ln \left(\frac{r}{1-r} \right) + \dots b_1 X_1 + b_2 X_2 + \dots$$

where r is age-, year-, sex-, race-specific proportional mortality rate for cause of death of interest, in U.S. national population;
 X_i is cumulative exposure in category i
 a_0, b_i , are effect coefficients to be estimated.

Models were fitted for the major associations described from SPMR analyses and were largely guided by those results. The age/year covariate was included obligatorily. The contribution of each risk factor to the final model was assessed by removing that one variable and computing a one-tailed P-value for the change in $2\log(\text{likelihood})$, which is approximately distributed

as chi-squared, with one degree of freedom.⁽³²⁾ Summary statements of estimated odds ratios, from logistic regression, were usually given as the odds ratio with respect to five years' latency- (and period-) weighted duration of exposure, and test-based confidence intervals were computed.⁽³²⁾

Analyses, both SPMR and logistic regression, were restricted to white workers, the deceased non-white population being too small for meaningful analysis (n=2).

RESULTS

Study Population

A total of 414 deaths were identified, constituting candidates for the study population. Figure 1 summarizes the steps taken in specifying the study population. The qualifying study population numbered 297, and all but 10 had cause of death information (96.6 percent). Those excluded consisted largely of workers whose date of hire was too close to their date of death for them to accumulate a latency-weighted duration of employment exceeding four years. Several others excluded were known to be non-hourly employees (supervisors).

The location of birth was obtained only for deaths for which death certificates were obtained (as opposed to death information from the Michigan death registry). For the 116 deaths with known location of birth, 4 had been born in Holland, and 6 others were non-U.S. born.

The distribution of the study population by age of death and year of death is given in Table 3, and the distributions of date of hire, termination, and death in major departments are given in Tables 4, 5. The majority of men in the study population were hired after 1950, largely in the period 1950-55. Half of the women in the study population were hired in the period 1942-44, probably for war production, and another third in the period 1950-55. Approximately 70 percent of the men and women terminated employment by 1970.

A work history consisting of one or more matches to seniority lists was available for the entire study population. The cumulative durations of time spent in major departmental groups is shown in Table 6. Most work by women was in the assembly departments, while men worked predominantly in machining, other fabrication, and maintenance departments. While only 5 of 210 men spent time in motor assembly, 22 of the 75 women did.

When exposures prior to 1960 were given special weighting (because of the apparent concentration of several specific cancer-site deaths prior to 1980), the cumulative exposures in various departments were as given in Table 7. The biggest reductions in cumulative duration caused by emphasizing the period pre-1960 are in those activities that expanded over time — e.g., micro-electromechanical assembly and electronic assembly — while the smallest reductions were for activities that were curtailed following the 1950s — e.g., motor assembly and instrument assembly.

The exposure experience of the study population in the five broad categories constructed across all job classifications and departments is summarized in Table 8. Solvent exposure in cumulative durations, weighted both for latency and for pre-1960 experience, was extensive for both men and women, although not necessarily consisting of high exposures relative to industrial hygiene standards. Epoxy and related resins in analogous materials were widely used by women of the study population (89 percent had some usage) but substantially less by men (only 37 percent had some usage). The cumulative duration in jobs where fast-curing adhesives and sealers were used

was somewhat less extensive than for epoxy-like exposures and, again, women were more extensively exposed. Only 28 percent of men had work involving soldering and flux exposures, while 53 percent of women did, and roughly 10 percent of women had more of this kind of exposure than virtually any of the men. Cutting fluid exposures, arising from most machining or grinding operations, were primarily experienced by men: 52 percent had some cumulative duration in cutting fluids while only 11 percent of women did.

To describe the migration of workers between different departments, counts were made of transfers between departmental groups indicated by consecutive matches to the five seniority lists (at three-year intervals). Figure 2 indicates that women workers tended to leave motor/winding departments and instrument assembly, and enter electromechanical and micro-electromechanical assembly. Women in the paint, inspection, and fabrication departments tended to stay in those departments. For men, there was migration from the salvage department, model shop, and the experimental model shop into machining, and migration out of machining to the flex shop (power actuator production), to other fabrication departments, to the tool departments, inspection departments, and the skilled maintenance departments (Figure 3). Stores, painting, and heat treat departments all had little exchange with other departments.

Standardized Proportional Mortality Analysis

The standardized proportional mortality ratios (SPMRs) for selected causes in the 210 white men of the study population are given in Table 9. The one notable elevation was for cancer of the pancreas ($\text{SPMR}=7/2.58=2.7$, $p=.03$). The all-cancer SPMR was .91 and that for atherosclerotic heart disease was 1.18. SPMRs for the 75 white women are given in Table 10. The all-cancer SPMR was significantly elevated ($\text{SPMR}=36/21.9=1.64$, $p < .001$) and the SPMRs for cancer of the colon, pancreas and stomach were all substantially elevated (colon: $\text{SPMR}=6/2.32=2.59$, $p=.06$; pancreas: $\text{SPMR}=4/1.0=4.0$, $p=.04$; stomach: $\text{SPMR}=3/.63=4.79$, $p=.05$). There were 7 deaths due to cancer of the ovary (ICD-8: 183.0). For the ICD-8 group of causes of death 183.0 to 184.9 (which includes the sites fallopian tubes and broad ligaments (183.1), unspecified (183.9) and other unspecified genital organs (184.0-184.9)), the expected number of deaths was 1.69. Therefore the SPMR for the ovarian cancer cases was greater than $7/1.69=4.14$ ($p=.004$) because the ovarian site is one of several possible.

When the observed cancers in excess in both men and women were examined in relation to year of death, all of the excesses occurred in the period 1965-1979 (Table 11). For the period 1980-83, the expected numbers are comparable to those in the two five-year periods 1970-79, but no pattern of excess proportions of deaths was observed for 1980-83.

For men with one or more months of epoxy exposure (latency-weighted and emphasizing pre-1960 exposures), a substantial concentration of the pancreas cancers (five out of seven) was observed, $\text{SPMR}=5/.97=5.2$, $p=.006$ (Table 12). Two of the cancer of the pancreas cases occurred in a small group with duration in inspection jobs ($n=36$, $\text{SPMR}=2/.45=4.5$, $p=.15$). For a variety of

other subpopulations (solvent use, cutting fluids, machining, fabrication, maintenance, tool work, etc.) there was no excess cancer of the pancreas.

When SPMRs for subpopulations of women were calculated, several associations were found. These selected subpopulations overlapped considerably. The 26 women with the longest latency-weighted durations in motor assembly or winding departments prior to 1960 had SPMRs for cancers of the stomach and pancreas considerably larger than for the group of all women (Table 13); for all digestive cancer deaths, 6 were observed for 1.80 expected (SPMR=3.34, $p=.02$). When the selection for motor/winding duration was based on latency-weighted durations over the full period 1940-1975, the same cancer sites showed slightly larger elevated SPMRs.

SPMRs for women with the greatest pre-1960 durations in epoxy-like exposures show a strong association with cancer of the colon, SPMR=5/.82=6.08, $p=.003$ (Table 14). When women were selected for exposures to cyanoacrylate-like materials, three pancreatic cancers were observed where 0.49 were expected (SPMR=6.1, $p=.03$), and 4 ovarian observed for 0.86 expected (SPMR=4.6, $p=.02$). (Table 15) In addition, 3 ovarian (SPMR=3/.38=7.9, $p=.01$) and 1 pancreatic cancer case occurred in the small group of deaths of women in inspection jobs ($n=10$). The SPMR results are summarized for the major exposure groups of interest in Table 16.

In order to assess the impact of the latency-weighting procedure on the selection of the study population and on the construction of the cumulative exposure measures, a second, extended population was defined consisting of the study population together with those candidates excluded solely because of the latency criterion. (Table 17) In general, for the key causes of death in women and men, the SPMRs estimated were slightly larger for the study population defined with weighted durations than for the extended population. When exposure groups in the study population are compared with those in the extended population (the latter selected using unweighted exposure durations, and requiring 20 or more years from date of hire until death, for latency), the effect estimates are larger for the study population (for colon cancer with epoxy and ovarian cancer with electromechanical assembly, in women; for cancer of pancreas with epoxy, in men). (Table 17)

Short Latency Malignancies

Because the latency-based selection and exposure measures were designed for long-latency diseases, the possibility of shorter latency malignancies was examined with the "extended" population (study population plus those excluded by the latency criterion). For men, there were 4 leukemias (ICD-8: 204-205) where 1.86 were expected (SPMR=2.15). Two of the leukemias were lymphatic, two were myeloid; there was one acute and one chronic disease of each type.

For women, there were five lymphopoietic cancer deaths (SPMR=2.6) in the extended population versus four (SPMR=2.3) in the study population. Three of the five cases were lympho- and reticulo-sarcomas (ICD-8:200; SPMR=3/.42=7.2, $p=.02$), and all three had spent time in electromechanical or

micro-electromechanical assembly. Forty-three of the 81 women in the extended population had spent some time in the EM/micro-EM departments.

In the population defined without latency weighting, there were two deaths of female workers caused by brain cancer ($PMR=2/.62=3.2$, $p=.04$, one-tailed test); this is one of the sites for which excesses had been hypothesized a priori. One of the two cases was included in the latency-based selection, the other missed selection by two months (a weighted duration of 46 versus the minimum required 48).

Mortality Odds Ratio Analysis

Because there were associations among the various exposure measures themselves, and in order to estimate selection and duration effects, logistic regression analyses of mortality odds ratios were undertaken, examining different exposure measures simultaneously, while adjusting for confounding by age and year of death. These analyses were guided by the SPMR results.

Cancer of the Colon in Women

When cases of colon cancer and controls (all other deaths) are examined in contingency tables, the association observed for exposures to epoxy-like materials (compared with unexposed) was not statistically significant, despite the 2.6-fold overall excess (Table 18). There were only eight unexposed in the population.

When the odds of a cause of death being colon cancer versus all other causes was modeled using cumulative exposure measures weighted for both latency and pre-1960 exposures, the exposure category most associated was that of epoxy-type materials, as suggested by the SPMR results. (Table 19, Model 1) The estimated mortality odds ratio for the epoxy-like exposure effect was 3.5 ($p=.009$, 95 percent $CI=1.2, 10$) for 5 years (weighted) duration at exposure level = 4 (in the 0,1,2,4,8 series). The standardized mortality odds ratio estimated for the unexposed population, compared with the U.S. population, was 0.68, an unstable estimate due to the small number of unexposed workers.

The soldering/flux exposure measure was also associated with colon cancer death but less than the epoxy measure (Model 5); when both were included (Model 7), the epoxy measure effect was slightly reduced compared to when it was the only exposure; the soldering/flux estimate was reduced and no longer statistically significant when both exposures were included. Jobs with soldering work, primarily in electronic assembly, usually were also coded as epoxy-exposed jobs. The effect estimated for age at death was nil. (Table 19, Model 9)

Transformations to diminish high values of the exposure measure for epoxy-like or related materials were computed because of the likelihood that high values reflected early initial employment in the period 1940-1950, when epoxy materials were not yet in wide use. Although the square-root transformed measure showed slightly greater statistical significance (Model 2), the intercept

estimate was clearly inappropriately small (adj. OR=.19) and the exposure effect estimate correspondingly inflated. A similar result was obtained for a truncated epoxy exposure measure (Model 3).

The goodness of fit of the final model is indicated in Table 20 where the population is stratified on the epoxy-like materials exposure measure, and the predicted number of colon cancer deaths based on the fitted model is compared with the observed. The estimated odds ratios for the exposure strata (relative to the unexposed) range from 1.14 to 10.7.

When latency-weighted exposures to epoxy-like materials were calculated without emphasizing pre-1960 exposures and substituted in the final model, the epoxy effect estimate was smaller (.0036 vs .0053) and less certain ($p=.02$ vs $p=.009$). When the same model was fit in the extended population, using unweighted cumulative exposures, there was no exposure effect for epoxy-like materials.

Cancer of the Ovary

No crude association was found between deaths due to ovarian cancer and exposures to materials used in electromechanical assembly, which included cyanoacrylates (Table 18). However, with logistic regression, a statistically significant effect was found for the square-root transformed cyanoacrylate exposure (Table 21, Model 1); the corresponding model using duration in electromechanical and microelectromechanical departments was similar (Model 6). In neither case was the association very certain; the estimate for the cyanoacrylate effect had a one-tailed P-value of .04; the 95 percent confidence interval was (.76, 67). The estimated mortality odds ratio for cyanoacrylate-like exposures was 7.2 for 5 years (weighted) duration at exposure level = 4. Another larger and more significant effect appeared with duration in inspection departments (also square-root transformed, Model 1). The estimated odds ratio for 5 years' duration was 11.9 ($p=.005$, 95 percent CI=1.8, 80).

The goodness of fit for the model relating ovarian cancer and exposures to cyanoacrylate-like materials and inspection jobs is indicated in Table 22. The joint confounding by age and year of death is positive for the lower exposure strata (an increase in expected of up to about 35 percent) but negative in the highest exposure stratum (expected diminished by 30 percent compared with unexposed stratum). The predicted stratum odds ratios' range is 1.9-15. Two of the ovarian cancer deaths had substantial work duration in inspection departments; they make up the cases in the stratum of zero-exposure to cyanoacrylates-like materials and account for the five-fold larger predicted versus expected in that stratum.

When latency-weighted exposures calculated without emphasizing pre-1960 exposures were substituted in the final model, the effect of exposures to cyanoacrylate-like materials and the inspection duration effect were smaller and less certain. Using the extended population and unweighted cumulative exposures, the cyanoacrylate-like effect was not statistically significant; the inspection effect was smaller than with the weighted measures but was still statistically significant.

Cancer of the Pancreas

The SPMR analysis and contingency tables (Table 18) suggested an association of cancer of the pancreas with exposures to epoxy-like materials in men. Logistic regression modeling suggested associations with cumulative exposure to epoxy-like materials and with duration in inspection departments, but these associations were uncertain ($p=.1$) (Table 23, Model 3). However, when the epoxy exposure measure was truncated (all values greater than 100 exposure-months being set equal to 100), in order to discount pre-1950 employment, a highly significant result was obtained (Model 1). The estimated mortality odds ratio for exposures to epoxy-like materials was 16, for 25 months (weighted) duration at exposure level = 4 (100 exposure-months), with a 95 percent confidence interval of (1.6, 163). There was no indication of association of pancreatic cancer with solvent use, exposure to cyanoacrylate-like materials or cutting fluids, or with durations in machining or fabrication departments.

The goodness of fit is displayed in Table 24. The two pancreatic cancer deaths with substantial inspection duration fell in the level of zero epoxy exposure and in the lowest exposed level. The odds ratios, by strata, range 2-16.

When exposure to epoxy-like materials (truncated) and duration in inspection both weighted to account for latency, but not emphasizing pre-1960 exposures, were substituted in the final model, the inspection effect vanished, but the epoxy effect remained ($p=.006$). Using the extended population and unweighted cumulative exposure measures, the inspection effect was again absent and the epoxy effect still quite significant ($p=.007$); the estimated effect corresponds to an odds ratio of 7.9 for 100 exposure-months.

The number of pancreatic cancer cases in women was too few to analyze ($n=4$). Although three of the four had some exposure to epoxy-like materials, only one had a relatively high cumulative exposure (with or without emphasizing pre-1960 exposures). When men and women were combined in logistic regression analysis, no common associations with pancreatic cancer deaths were found except for a weak association with duration in inspection departments.

Confounding By Ethnic Factors

In order to assess whether there was likely confounding in this study due to the high proportion of Dutch ancestry in the county, a comparison was made between Kent County and Genesee County, another Michigan county with a medium-sized city and a mixed industrial base but without an elevated proportion of Dutch ancestry. Using the computerized state death registry, all deaths for cancer of the pancreas, colon and ovary, together with referent causes of death consisting of most malignant and non-malignant causes, were selected for the years 1970-82. Mantel-Haenszel odds ratios were computed comparing the two counties on the odds of deaths due to the cause of interest versus selected other causes. Deaths were stratified on 10-year age intervals and 5-year year-of-death intervals. The results are shown in Table 25. For colon cancer, the most common of the causes of death examined, the Mantel-Haenszel odds ratio for women was 1.01, implying the two counties are

indistinguishable. For cancer of the pancreas, the odds ratios differed from 1.0 but were not statistically significant (for women: OR=1.17; for men: OR=1.07). However, for cancer of the ovary and related diseases (ICD-8:183.0-183.9), there was a statistically significant elevation in odds of dying from ovarian cancer in Kent County: OR=1.37; 95 percent CI=1.14,1.64.

LITERATURE REVIEW

Potential Carcinogenicity of Specific Agents

A survey of hazardous exposures and known health effects for the contemporary electronics and microelectronics industry has been published by NIOSH.⁽³³⁾ The agents described in the following paragraphs were used at this plant to at least some degree during the period of employment of the study cohort at risk. Information on usage was obtained by reviewing available industrial hygiene records, interviewing plant personnel, and reviewing past and current material safety data sheets. Specific usage has included: carbon tetrachloride, perchloroethylene, and 1,1,1-trichloroethane as general purpose solvents and degreasing agents; chloroform in die and wire bonding and assembly; epoxy resin systems, cyanoacrylate-based adhesives, and plastics, sealants or adhesives containing acrylonitrile or butadiene in various assembly operations. Early resin systems used in injection molding prior to 1960 probably included phenol-formaldehyde. Early electric motor fabrication may have involved use of coal or asphalt-derived tars for insulation and potting media.

Solvents/Degreasers

Carbon tetrachloride. Administration to various strains of rats and mice by a variety of routes (oral, subcutaneous, inhalation) has produced liver tumors including hepatocellular carcinomas.⁽³⁻⁶⁾ In one experiment, subcutaneous injection produced a significant excess of mammary adenocarcinoma in rats.⁽⁷⁾

Three human cases of liver cancer following acute exposures have been reported.^(8,9,10) A case-control proportional mortality study of workers dying from lymphocytic leukemia exposed to any of 20 solvents in the rubber industry found the highest odds ratio (14.8) for carbon tetrachloride.⁽¹¹⁾ In a proportional mortality study of 330 deceased laundry and dry cleaning workers who had been exposed to carbon tetrachloride, trichloroethylene and perchloroethylene, a statistically significant excess of lung (PMR=17/10=1.7), cervical (PMR=10/4.8=2.1) and skin (PMR=3/.7=4.3) cancers, and a non-significant excess of leukemias (PMR=5/2.2=2.7) and liver (PMR=4/1.7=2.3) cancers were observed.⁽¹²⁾

Perchloroethylene (tetrachloroethylene). Administration in corn oil by gavage in B6C3F1 mice produced a significant excess of hepatocellular carcinoma in both male and females.⁽¹³⁾ Relevant human data includes the study of dry cleaning workers cited above.⁽¹²⁾

1,1,1-trichloroethane. There has been a negative NCI study, but it was difficult to interpret because of excessive mortality among control and dosed animals.⁽¹⁴⁾

Chloroform. A National Cancer Institute feeding study found a significant increase in renal epithelial tumors in rats and a highly significant increase of hepatocellular carcinomas in mice.⁽¹⁵⁾ Another feeding study found a significant increase of renal tumors in a different strain of mice.⁽¹⁶⁾

Polymerization Systems

Epoxies. Typical epoxy resins have contained epichlorohydrin, bisphenol A (a polyhydroxy compound), and a variety of epoxides; "hardeners," or cross linking agents, have included polyamines, acid anhydrides, and polybasic acids.⁽¹⁷⁾ Noncross-linking catalysts include various polyamides, monoethylamine, and tertiary amines. Diluents — phenyl, allyl, and butyl glycidyl ethers, styrene oxide, styrene, and other epoxides may be utilized to reduce viscosity.⁽¹⁸⁾ Inhalation of epichlorohydrin produced a significant excess of squamous cell carcinomas of the nasal cavity in Sprague-Dawley rats.⁽¹⁹⁾ In a prospective study of 35 workers occupationally exposed to epichlorohydrin, a significant increase in lymphocyte chromosomal aberrations was observed.⁽²⁰⁾ A standardized mortality study of 864 workers occupationally exposed to epichlorohydrin found a significant increase in deaths due to respiratory cancer.⁽²¹⁾ Information on smoking histories and other chemical exposures was not available. The carcinogenic effects observed for various epoxides have been reviewed by Patty.⁽¹⁷⁾

In a proportional mortality study of workers employed 10 or more years in helicopter production, including those fabricating rotor blades using epoxy resins and the hardener methylene dianiline (MDA), a statistically significant excess of colon cancer was observed ($PMR=15/8.6=1.74$, $p=.03$, one-tailed test);⁽²²⁾ in the group ever exposed to epoxy systems, the PMR was $7/3.1=2.26$. Also elevated was the proportion of bladder cancer ($PMR=3/.8=3.7$, $p=.05$), lymphosarcoma ($PMR=3/.87=3.5$, $p=.06$), and skin cancer ($PMR=3/.88=3.4$, $p=.06$) deaths.

Synthetic Rubber Components. The major use of acrylonitrile in the electronics industry is as a co-polymer with styrene and butadiene in rubbers and adhesives. A 1978 Manufacturing Chemists Association study produced a significant excess of tumors (stomach papillomas, central nervous system tumors, zymbal gland carcinoma) in rats when acrylonitrile was administered in drinking water.⁽²³⁾ Male and female rats exposed by inhalation demonstrated an excess of CNS, ear canal, and mammary tumors. A Dupont cohort study of 470 male polymerization workers with occupational exposure to acrylonitrile and greater than 20 years latency found a significant excess of lung cancer and colon cancer.⁽²³⁾ Smoking habits were not reported. Butadiene has been reported as a strong carcinogen in rats⁽²⁴⁾ causing malignant lymphomas, squamous cell neoplasms of fore-stomach, hemangiosarcomas of the heart, mammary tumors and ovarian and liver neoplasms at 625 and 1,250 ppm after 60 weeks. (The current OSHA standard for butadiene is 1,000 ppm and rulemaking has been proposed.⁽²⁵⁾)

Methyl 2-cyanoacrylate. The major use in the electronics industry is as a base for quick-curing adhesives. Bacterial mutagenicity testing of two commercial adhesives (TIXO K100 of Hapas and Cyanolite 102 of 3M) containing methyl 2-cyanoacrylate demonstrated dose-dependent reversion of histidine dependent Salmonella typhimurium strain TA 100.⁽²⁶⁾ Further testing established that the monomeric vapor was responsible for reversions. No animal or human data is available on this substance.

Tar-based Materials

Besides the extensive literature on the carcinogenic hazards of coal tar emissions from coke ovens,⁽³⁴⁾ studies in aluminum smelters where tar-aggregated carbon electrodes are produced and consumed at high temperatures imply carcinogenic risks. In a cohort of 22 thousand workers at 14 reduction plants, cancer of the pancreas was statistically significantly elevated (SMR=1.97, $p < .05$) for potroom workers of 20 or more years' duration.⁽³⁵⁾ There was a nonsignificant excess of stomach cancer as well. In another study with a cohort of 5,400, there were elevations for stomach and esophageal cancer, bladder, and lung cancer.⁽³⁶⁾ Tar-related exposures may have been experienced in armature winding and other jobs involved in small electric motor production (for actuators, gyroscopes) in the present study.

Solders/fluxes

Rosin core solder pyrolysis products. Colophony or gum rosin, the residue remaining after turpentine has been steam-distilled from oleoresin obtained from long leaf and slash pine, is used in rosin core solder. The flux contains an amine hydrochloride activator which liberates hydrochloric acid when heated.⁽³⁷⁾ Thermal decomposition products which may be generated during soldering include acetone, methyl alcohol, formaldehyde and other aliphatic aldehydes, carbon dioxide, carbon monoxide, methane, ethane, abietic acid and related diterpene acids.⁽³⁸⁾ Among these pyrolysis products, formaldehyde is a carcinogen. Two different formaldehyde inhalation studies found a significant excess of squamous cell carcinoma of the nasal cavity in rats.^(39,40) Several studies have demonstrated excess brain cancers and leukemia among professional workers (pathologists, anatomists) exposed to formaldehyde and other chemicals.⁽⁴¹⁾

Epidemiology of Ovarian Cancer

Cell types. Among adults in western industrialized countries greater than 90 percent of ovarian cancers are of epithelial origin.^(42,43) The most common epithelial cell types in roughly descending order of frequency are: serous cystadenocarcinoma, endometrioid carcinoma, mucinous cystadenocarcinoma, and clear cell carcinoma. Granulosa cell carcinoma is the most common non-epithelial ovarian malignancy among adults.

Incidence. Cancer of the ovary will affect 1 to 2 percent of caucasian women and will cause death in most of them.⁽⁴⁴⁾ Incidence is highest in Northern Europe and lowest in non-industrialized countries and Japan, ranging from a high 14.9 cases per 100,000 women per year in Sweden to 4.6 in India and 2.7 in Japan.⁽⁴⁵⁾ Rates from the Netherlands were not reported. In the United States incidence is higher among whites (14.2) than among blacks (9.3).⁽⁴⁶⁾ U.S. death rates among white women from 1950 to 1969 were higher in the Northeast than other regions of the country. Death rates for cancer of the ovary for Japanese migrants in Hawaii and their first generation offspring are significantly higher than those in Japan.⁽⁴⁷⁾

The incidence of cancer of the ovary rises steeply from early adulthood until age 70⁽⁴⁷⁾. Both this age distribution and worldwide incidence trends are similar to other tumors of epithelial origin including breast, prostate, colon, and endometrial.

Carcinoma of the ovary versus other malignancies. Epithelial tumors metastatic to the ovary (most often of colonic or gastric origin) may be difficult to distinguish from primary ovarian tumors. Estimates of the fraction of female patients with colon carcinoma who will develop ovarian metastases range from 1.4 to 8 percent^(48,49). Women who have been treated with alkylating agents for ovarian carcinoma are at markedly elevated risk for developing acute non-lymphocytic leukemia (5.8 cases per 1000 women per year).⁽⁵⁰⁾ With respect to asbestos exposed populations, the difficulty of distinguishing metastatic ovarian carcinoma from peritoneal mesothelioma may present diagnostic problems.

Non-occupational risk factors. Risk factors which have been strongly associated with epithelial neoplasms of the ovary include early menopause, late menarche, nulliparity (especially in married women who failed to conceive), fewer pregnancies, a prior history of breast cancer, and — only for endometrioid carcinoma — obesity and hypertension⁽⁴⁴⁾. Among women aged 40-65, prior use of oral contraceptives was associated with decreased risk.⁽⁵¹⁾ These associations have generated the hypothesis that decreased production of sex hormones by the ovary leading to failure of feedback inhibition of pituitary gonadotropin production, and thus unopposed ovarian stimulation, may be a common causal pathway.

Because of the association of parity and other reproductive factors with the incidence of cancer of the ovary and breast, it has been suggested that elevated PMRs for ovarian cancer in industrial populations may simply reflect different reproductive behavior, e.g., deferred child bearing. A study attempting to address this issue found supporting evidence, although important social class factors were not controlled for.⁽⁵²⁾

Several studies have failed to demonstrate an association of ovarian cancer with alcohol consumption or with tobacco use.^(53,54) In one case-control study it was found that ovary cancer patients consumed significantly more coffee than matched controls.⁽⁵⁵⁾ Sweden has both the world's highest incidence of ovarian cancer and highest per capita coffee consumption.⁽⁴⁴⁾

Most hypotheses about an association of ovarian cancer with diet have focused on high intake of meat and animal fats. However some evidence is in conflict with this hypothesis: Utah Mormons, who do eat meat and animal fats, have lower rates than Utah non-Mormons;⁽⁵⁶⁾ British women members of two religious orders who eat little or no meat have the same rates as other British women.⁽⁵⁷⁾

Environmental Agents and Ovarian Cancer

Animal Studies. Several chemical carcinogens, most notably polynuclear aromatics (20-methyl-cholanthrene and 7,12-dimethylbenz(a)anthracene), have

induced ovarian neoplasms in rodents.^(58,59) Most of these neoplasms have not been of epithelial origin.

Human epidemiology. Particulate materials of the talc-asbestos group have received the most serious consideration as possible environmental etiologic factors in ovarian cancer. The most provocative evidence of a specific association with talc was the finding of talc particles deeply imbedded in 10 of 13 ovarian tumors studied.⁽⁶⁰⁾ A study of female workers with relatively short history in a talc factory found no excess of ovarian cancers.⁽⁶¹⁾ A recent case-control study suggested an association between ovarian epithelial cancers and cosmetic use of talc⁽⁶²⁾ (transvaginal route of entry was postulated).

Some studies have found an excess of ovarian cancer^(60,62) or of peritoneal neoplasms⁽⁶³⁾ among female asbestos workers. The similarity of metastatic carcinoma of the ovary — both in histologic appearance and embryologic tissue of origin (specialized mesenchymal cells) — to peritoneal mesothelioma has been cited as evidence in support of an asbestos association.

There are few other reports of an occupational association in the literature. A proportional mortality study of female cosmetologists and hair dressers in British Columbia found a excess of cancer of the ovary (8 deaths versus 3.9 expected, $p=.09$).⁽⁶⁴⁾ Among a cohort of 78 Swedish women occupationally exposed to an anti-rust oil containing N-phenyl-1-naphthylamine, 12 developed malignant neoplasms versus 3.9 expected. Two of these neoplasms were ovarian.⁽⁶⁵⁾

Epidemiology of Pancreatic Cancer

Cell types. Adenocarcinoma of the exocrine gland accounts for over 90 percent of all malignant pancreatic tumors.⁽⁶⁶⁾ Most demographic data do not distinguish histologic types.

Incidence. Pancreatic cancer, the fifth commonest cause of cancer death in the United States, accounts for more than 20,000 deaths annually.⁽⁶⁶⁾ It is almost uniformly fatal. In most populations, it is one and one-half to two times more common in males than females. Incidence rates tend to be highest in western industrialized countries ranging from 14.1 per 100,000 males per year in Finland to 11.7 in Connecticut to 5.7 in Cali, India. In the United States, incidence rates for black males are approximately double those for white males. Moreover the rate of increase in pancreatic cancer between 1948 and 1970 was substantially greater for blacks than for whites. The disease is rare in persons under forty. Thereafter the incidence rises steeply with increasing age.

Non-occupational risk factors. Cigarette smoking has been convincingly associated with cancer of the pancreas with heavy smokers demonstrating a two-fold increased risk.⁽⁶⁶⁾ It has been suggested that an observed association of pancreatic cancer with diabetes is mostly explained by the undiagnosed tumor itself causing diabetic symptoms. However, two studies which excluded cases developing diabetes shortly before the pancreatic cancer still found an association among women but not among men^(67,68). One large Japanese

follow-up study found persons who reported daily meat consumption had 1.5 times the risk of those who are meatless frequently.⁽⁶⁹⁾ Several large studies of various designs have failed to identify alcohol consumption as a risk factor.⁽⁶⁶⁾

The etiologic role of coffee consumption is controversial. One large case-control study found a significant association of pancreatic cancer with coffee drinking (odds ratio of 1.8 for 1 to 2 cups per day, 2.7 for 3+ cups per day).⁽⁷⁰⁾ In another study, while there was no difference between cases and controls in the percentage of coffee drinkers overall, there was a higher percentage of drinkers of decaffeinated coffee among cases.⁽⁷¹⁾ Several other studies,^(72,73) including another large case-control study,⁽⁷⁴⁾ have failed to confirm an association.

Occupational Risk Factors and Pancreatic Cancer

Animal Studies. Several chemicals, including a variety of nitrosamines, 7,12 dimethylbenzanthracene and 4-hydroxyamino quinolone-1-oxide, have induced pancreatic carcinomas in rodents. Diets high in fat often appear to act as promoters for these carcinogens.

Human epidemiology. A case-control study in Louisiana of pancreatic cancer in counties with elevated rates found an association with oil refining and paper manufacturing.⁽⁷⁵⁾ A different case-control study found a significant duration-of-exposure dependent increased risk among persons employed in dry cleaning, service stations, or auto garages.⁽⁷¹⁾ A five-fold elevated risk was present among persons with greater than 10 years of exposure. A proportional mortality study of members of the American Chemical Society found 56 deaths against 35 expected.⁽⁷⁶⁾ In a previous proportional mortality study conducted by the UAW at a bearing plant,⁽²⁾ machining and grinding using straight oil cutting fluids were associated with significantly increased risks for pancreatic cancer (odds ratios three or greater); at another bearing plant a smaller, nonsignificant elevation was present.⁽¹⁾ A NIOSH investigation at a electronics plant producing missile guidance systems found an excess of pancreatic cancer among white male hourly employees but not among white female hourly employees⁽²⁷⁾.

Epidemiology of Cancer of the Colon

Occupational and non-occupational risk factors for cancer of the colon have been reviewed previously.⁽²⁾ Briefly: the U.S. has the highest worldwide incidence of cancer of the colon, and the U.S. incidence has increased substantially over the past 30 years.⁽⁷⁷⁾ Dietary factors have been hypothesized to explain the marked increase in incidence observed among groups immigrating to the U.S. from countries with low rates (i.e., Eastern Europe).⁽⁷⁸⁾ Exposures or occupations which have been associated with an increased risk of cancer of the colon in some studies include machining,^(79,80) grinding,⁽⁸¹⁾ synthetic abrasives,⁽⁸²⁾ and an agent present during the production of polyester fiber for carpet production.⁽⁸³⁾

Previous Mortality Studies in the Electronics Industry

Both the 1970-1972 mortality statistics of England and Wales⁽⁸⁴⁾ and an American study⁽⁸⁵⁾ suggest an excess risk of pharyngeal and oral cancers among electrical and electronics workers. A study⁽⁸⁶⁾ of cancer incidence from 1961-1973 utilizing the Swedish Cancer Registry found a significant excess of cancer of the pharynx (age, social class adjusted relative risk=2.97, 95 percent CI=1.7, 5.1) and lung cancer (age, social class adjusted relative risk=1.36, 95 percent CI=1.2, 1.5) among male blue collar electronics or electrical manufacturing workers as compared to all other workers. Among "other electronic workers" which "contains a more unqualified and machine-bound group of workers, preoccupied with assembly type jobs (than the other two categories of electrical workers)," statistically significant excesses of oral cancers among males and cancer of the nasal cavities and lung among both males and females were observed.

A second Swedish study focused on three plants of a large telecommunications manufacturer.⁽⁸⁷⁾ No excess respiratory cancer was observed; however, there was a statistically significant elevated SMR for malignant melanoma (SMR=12/4.6=2.6). The skin cancer was associated with soldering work where the SMR was 3.9.

A NIOSH proportional mortality investigation⁽²⁷⁾ of deaths between 1950-1980 at an electronics plant producing missile guidance systems found among hourly female employees an excess of ovarian cancer (6 vs 2.4 expected, $p = .08$, two-tailed Poisson) and stomach cancer (4/.79=5.1, $p=.02$). Among male hourly workers, there was an excess of pancreatic cancer (6/2.6=2.3, $p=.10$) and brain cancer (5/1.64, $p=.05$).

DISCUSSION

Study Population

The identification of the cohort at risk for death is believed to be quite complete, because it is based on a pension system which appears to have been well managed. Annual reports provided a complete accounting of all time credited to employees. Both retirees and deferred vested employees are tracked.

Vital status determination beyond that indicated in pension records should be very complete for deaths occurring in Michigan because the cohort was searched against the state death registry. Although deaths among the deferred vested group occurring out-of-state before age 65 would likely be missing in the pension files, the search of the Social Security death file produced only 11 new deaths. Missed out-of-state deaths are likely to be fewer than 20, or 7 percent of the study population, given that only 11 were found in the search (representing all ages at death).

Cause of death information was acquired for all but 10 of the study population (3.4 percent). Therefore the analysis was carried out for a population believed to be greater than 90 percent complete (less than 7 percent undetected deaths, and 3 percent known deaths without cause of death information).

Exposure Classification

The classification of jobs and departments was based on incomplete historical information and only partially defined production activities, and the algorithm used to calculate joint job-department exposure levels and then aggregate them over time, taking into account latency, was based on reasonable but not uniquely determined choices. However, these choices were made prior to any systematic assessment of possible associations.

The construction of exposure categories across departments was essential, because there were small numbers employed in individual departments and there was substantial migration among departments; this construction was possible because the use of several broad categories of materials, such as solvents and epoxy-like materials, was common to several departments in roughly comparable activities.

Self-Selected Cluster

Because this study originated with a perception of increased cancer reported by the local union, there is the concern that the cluster of cancer deaths is simply a random cluster arising by chance. There are two considerations that mitigate against this concern. First, the originally perceived excess was never identified primarily with the female workers who ultimately comprised 25 percent of deaths but for whom most of the deaths making up the excesses were found. Second, the list of deaths and incident diagnoses

originally compiled by the local union and forming the basis of their concern included only one-third (31 percent) of the subsequently identified cases of cancer of the stomach, colon, pancreas, and ovary, the sites shown to have statistically significant excesses in the full study population.

Exclusions Based on Latency

The use of a weighting function to reduce the durations of time intervals contributing work history, depending on proximity to the date of death, was intended to exclude from the study population those least at risk for disease related to work at this plant. Approximately 17 percent of the male candidates for the study population were excluded by the latency weighting criterion, including 1 of 8 cancer of the pancreas cases; 7.5 percent of female candidates were excluded but none of the cases of interest (cancer of colon, stomach, pancreas and ovary).

Exclusion was chosen over stratification because the numbers excluded were small and because the study population candidates with small intervals between time of hire and death were more likely to have had significant prior employment at another employer. Unknown work history and possible exposure misclassification would result.

The specific form of the weighting function was somewhat arbitrary, depending on a very approximate estimate of average latencies for long-latency malignancies. This choice is no more arbitrary, and is biologically more plausible, than traditional approaches that implicitly utilize step functions rather than continuous functions in distinguishing high risk groups. For example, requiring a minimum of 10 years of duration and a date of hire at least 15 years prior to death is a selection that will include some individuals who are at lower risk than some of those excluded: a worker with 9 years of employment beginning 25 years prior to death is at higher risk for employment related, long-latency disease than one employed 11 years beginning 16 years prior to death.

Findings

The clustering of the elevations in proportions of deaths due to cancers of the colon, pancreas, stomach and ovary in the years 1970-1979 could have been a chance event; however, it was unlikely for this pattern to appear simultaneously for 4 distinct cancer sites in women, and for one in men, and for all those sites to be statistically significantly elevated over the entire study period (1958-1983).

The excess cancer proportional mortality in women does not appear to have been a general excess of all cancer, compared with nonmalignant causes of death: for the two leading causes of cancer death in U.S. women—lung cancer and breast cancer—the observed deaths were fewer than expected. If the cancer excesses were merely a consequence of an unusually low rate of circulatory disease, then all other nonmalignant conditions would be elevated, but they were not ($PMR=15/17.7=.85$). (Table 10)

The hypothesis that this cluster represents a time-delimited outbreak of work-related disease, primarily in women workers, is supported by the finding that associations of particular cancer outcomes with work histories are more certain when exposures prior to 1960 are emphasized. However because the numbers of cases for each outcome are small, the largest group numbering 7, and because specific prior hypotheses relating particular sites to particular exposures had not been defined, the findings of this study must be considered largely exploratory or hypothesis-generating, rather than confirmatory. For this reason statistical significance is not stressed for some of the less certain results.

Colon Cancer in Women

A woman who had exposure to epoxy-like materials could have worked in a variety of jobs and departments such as instrument assembly, electronic assembly, fabrication, painting, motor assembly and winding. The departments in which the 6 colon cancer cases acquired epoxy-like exposures, prior to 1960, were: motor assembly (2 cases), winding (1 case), electronic assembly (3 cases), instrument assembly (1 case) and painting (1 case); 2 cases had exposure in more than 1 department. The actual materials used could have differed across departments and over time, and process activities could have varied, e.g. whether materials were baked in ovens to speed curing. Furthermore, the putative causative agent or agents found to be associated with colon cancer may have been some material associated with epoxy resin use but actually quite different, for example particular solvents or fillers used with epoxy binders. The localization of the hypothesized carcinogen to the pre-1960s period suggests several possibilities: 1) early polymer systems containing carcinogens subsequently eliminated or reduced in content, 2) reduced but continuing use of the particular material or of materials containing the same agent(s) 3) changes in working environment, e.g. ventilation, work practices. There has been a substantial reduction in the proportions of activity devoted to motor assembly, instrument assembly, and armature winding since the 1950s. Changes in working conditions seem not to have been dramatic. Although clean-rooms for delicate assembly have rigorous control of particulate aerosols, they were designed primarily for protecting products (laminar flow hoods blow out to worker); organic vapors are not controlled. However, working conditions in these areas probably are substantially improved over earlier periods. The finding of a marginally significant positive additional effect of work in electronic assembly departments (Table 19) suggests that the agent responsible may have been present in these departments with higher relative exposures than accounted for by the exposure classification used in this study.

Although cultural factors, possibly represented by origin of birth, could not be evaluated directly, the case-control analysis comparing 2 Michigan counties reveals no general difference for colon cancer mortality odds, implying that Dutch ancestry is not confounding.

Ovarian Cancer

The carcinogen suggested by the ovarian cancer association could have been any material relatively unique to the electromechanical and micro-electromechanical assembly departments or related to inspection activities. Adhesive polymer systems such as cyanoacrylates are merely one example; cyanoacrylate-based materials were first used at this plant in the late 1950s or early 1960s and continue in use, according to plant personnel. The time localization of the ovarian cancer suggests that the prevalence of the causative exposure declined following the 1950s.

The departments in which the ovarian cancer cases were employed were: electromechanical (three cases), micro-electromechanical (one case), overhaul (one case), motor assembly (one case), winding (two cases), and inspection (three cases); four cases had more than one department. Two of the cases had exclusively inspection work history.

The finding of three ovarian cancer deaths (and one pancreas cancer) among the small number of women in inspection departments, together with the analogous finding for pancreatic cancer in men, requires reconsideration of the potential exposures involved in that work, much of which consists of detailed examination of parts or subassemblies used in subsequent assembly operations. The report published by Jahrvolm, *et al.*, concerning anti-corrosion oil additives and strong associations with epithelial cancers in women handling treated parts, may be relevant.⁽⁶⁵⁾

The case-control analysis of ovarian cancer between counties indicates that ovarian cancer is significantly more common as a cause of death in Kent County than in Genesee County and implies that using national proportional mortality rates understate the expecteds in the SPMR analysis, by approximately 37 percent. The estimated exposure effects would be correspondingly overestimated. However, the possibility that ovarian cancer is diminished in Genesee County cannot be ruled out; this could arise from higher rates of hysterectomy in that county. The logistic regression-based exposure effect estimates should be less affected by the use of inappropriate references rates because an internal exposure comparison was used.

The conjecture that female industrial populations have a higher risk of ovarian cancer due to deferred child-bearing⁽⁵²⁾ is not believed to be relevant in this study. The women in this study population were generally working mothers. Furthermore, there was no excess in breast cancer also thought to have the same parity-dependence. In another study, in a machining population with 220 deaths in females,⁽²⁾ there was no excess for cancer of the ovary (PMR=2/3.8=.53) and an insignificant excess for cancer of the breast (PMR=13/10.5=1.24).

Pancreatic Cancer

There was an excess proportion of deaths due to cancer of the pancreas in this study population that was very unlikely to have occurred by chance. In men and women combined, 11 cases were observed for 3.6 expected ($p=.0025$,

Poisson, two-tailed). SPMR and SMOR analyses suggested an association with epoxy-like exposures in men. The model using the truncated exposure measure for epoxy-like materials suggests that early exposures, in the period 1942-1950, were not part of the association, further supporting the hypothesis that chemicals introduced and used in the 1950s were the causative agents. Another exposure possibly shared by male workers working with epoxy-like materials was that arising from injection molding, probably with phenol-formaldehyde systems. However, only one of the white male pancreatic cancer cases had a work history which included the molding job classification.

The group of men and women with the highest SPMR was workers with several years in inspection activities: 3 pancreatic cancer deaths where 0.56 were expected, in this group of 44 men and women. The actual departments worked in, for the 3 cases, were: machine shop parts inspection, model shop inspection and inspection-repair.

More women than men had high cumulative exposures to epoxy-like materials, based on the exposure measure constructed. If the association observed for men reflects a true causal relationship, if both men and women have similar susceptibility, and if the exposure measure is consistent between men and women, then more women with high epoxy-like exposures would be expected to have died from cancer of the pancreas than were observed in this study (expected age-specific proportional mortality rates are similar between men and women). This implies that some of these assumptions are invalid; it is probable that the category of exposures to epoxy-like materials actually reflects exposures to different materials for men and for women, due to differences in their job characteristics. However, there was an overall four-fold excess of pancreatic cancer deaths in women, and the SPMR results indicate these deaths were concentrated in jobs with exposures to cyanoacrylate-like materials.

Because cancer of the pancreas does not differ between Kent and Genesee Counties, confounding due to Dutch ancestry or other regional, cultural factors is not likely to be affecting the findings for cancer of the pancreas.

Lymphopoietic Malignancy

This study has insufficient power to conclude that excess leukemias or lympho/reticulo-sarcomas have occurred, despite excesses of two-fold or more in the SPMRs. The suggested association of sarcomas with electromechanical assembly jobs in women requires further investigation in other populations.

Relation to Previous Studies

Some of the findings of the NIOSH Health Hazard Evaluation at Delco Electronics, Milwaukee⁽²⁷⁾ are similar to the findings in this study. Excess proportions of deaths due to cancer of the stomach and cancer of the ovary were seen for women in both populations. Cancer of the pancreas was elevated for men in both studies. Another major finding in the Delco study was the

statistically significant excess of brain cancer in men ($SPMR=5/1.64=3.05$ in hourly, $4/1.35=2.96$ in salaried); in women at Delco, there were 2 brain cancer deaths for .99 expected. In this study there were no brain cancer deaths in male workers, but there was a comparable excess in women ($PMR=2/6=3.2$, in the extended study population). While not statistically significant, this is limited support for an occupational etiology for increased brain cancer in electronics production. The elevated cancer of the colon and pancreas seen for women in the present study was not observed at Delco.

Analyses of work histories at the Delco plant were not sufficient to examine in detail particular classes of chemical exposures relating to production. Although the final products for the Delco plant and the current study plant were very similar, production differed. At Delco many components for assembly are manufactured elsewhere, whereas at Lear Siegler most basic components such as gyros, motors and frames are manufactured in the plant. In the past, production may have differed very substantially in the two plants. Lear Siegler was involved in aircraft instruments and radio production dating from the 1940s, while Delco entered avionics (aircraft instruments) manufacturing somewhat later, in the 1950s. Details and relative composition of production could have differed widely between the two plants, as could the distributions of men and women in different jobs.

An association between brain cancer and work in the electrical industry has been observed in several other studies. Lin, et al., review these studies and also report a similar finding in a population-based death certificate case-control study.⁽⁸⁸⁾ Based on 519 matched pairs, a statistically significant odds ratio of 2.15 was obtained comparing the highest electromagnetic field exposure stratum with the unexposed. An association with electromagnetic field strength was concluded, although confounding chemical exposures were not ruled out.

Studies in rats have found stomach cancer and also CNS tumors associated with acrylonitrile.⁽²³⁾ A cohort of chemical production workers with acrylonitrile exposure had significant excess of colon cancer.⁽²³⁾ Non-epithelial ovarian cancers have been observed in rodents associated with polynuclear hydrocarbons,^(58,59) and a small study of women exposed to complex aromatic amines present in antirust oils found elevated ovarian cancer (two cases).⁽⁶⁵⁾ A case-control study of dry-cleaning workers (presumably exposed to chlorinated hydrocarbons) found a five-fold risk of pancreatic cancers.⁽⁷¹⁾ All of these exposures were potentially present in the study plant, where the same causes of death in excess were observed. The specific carcinogens responsible cannot be identified in this study.

CONCLUSIONS AND RECOMMENDATIONS

Findings

There is evidence that a time delimited outbreak of occupationally-associated cancer deaths has taken place in this study population. In the period 1965-1979, 30 cancer deaths occurred in women workers, when 15.5 were expected based on national proportional mortality rates (Table 11). Almost half of the deaths for women over the entire study period were due to cancer, the sites in excess being colon, ovary, pancreas and stomach. For men, there was an excess of cancer of the pancreas for the same period. Over the last four years of the study, 1980-1983, there is no evidence of increased cancer in men or women; however, the small numbers make this conclusion uncertain.

Specific associations were found with broad categories of exposure, most clearly for cancer of the colon and epoxy-like materials and for cancer of the ovary and inspection work. Chemicals used in motor production, electromechanical assembly and/or painting are implicated by these findings, but the specific identities cannot be indicated beyond the broad categories used. Nevertheless the widespread use of a variety of halogenated solvents and of reactive resin systems of several kinds makes these materials suspect. Moreover, other agents may have been important, especially materials used in the 1950s or before. Exposures that took place in some inspection activities are also quite suspect. In the nine deceased women who were estimated to have spent a year or more in inspection jobs prior to 1960, there were three deaths due to ovarian cancer and one due to pancreatic cancer. Men in inspection showed an association with death due to cancer of the pancreas.

The likely occurrence in this population of cancers attributable to chemical exposures demonstrates the need for thorough characterization of hazardous exposures, explicit communications of hazard to workers exposed, and the institution of adequate controls. In the absence of sufficient knowledge about potential hazards, appropriate prudent assumptions should be made and acted upon.

Recommendations

These results are largely exploratory in nature, indicating some important hypotheses to be examined in other populations. However, some of the associations are strong enough to merit serious concern and critical examination of past and present industrial hygiene controls. The following recommendations are made based on this study as well as on general observations of the current production activity:

1. An independent industrial hygiene assessment of current production is needed with specific attention to (a) local exhaust ventilation to be provided for most assembly operations, including electronic, electromechanical, winding, etc.; (b) handling of resin systems, including mixing, curing, grinding, etc.; (c) use of solvents in

fabrication and assembly; (d) controls of cutting fluid exposures in machining and grinding applications.

2. A hazardous materials control committee should be established with union participation for the purpose of reviewing all materials used and establishing appropriate production practices and control where not already in place.
3. A detailed reconstruction of exposures is needed for some specific activities as they were carried out in the 1950s: motor assembly and winding, electromechanical assembly, and inspection jobs. Emphasis should be placed on early polymer systems and their predecessor materials. This will require in-depth interviews with staff and workers for that period and examination of examples of actual products from that period and their production specifications. Early polymer product composition information should be obtained from manufacturers.
4. The major findings in this study should be examined in another similar population.
5. Continued surveillance to determine if period of excess risk is truly over.

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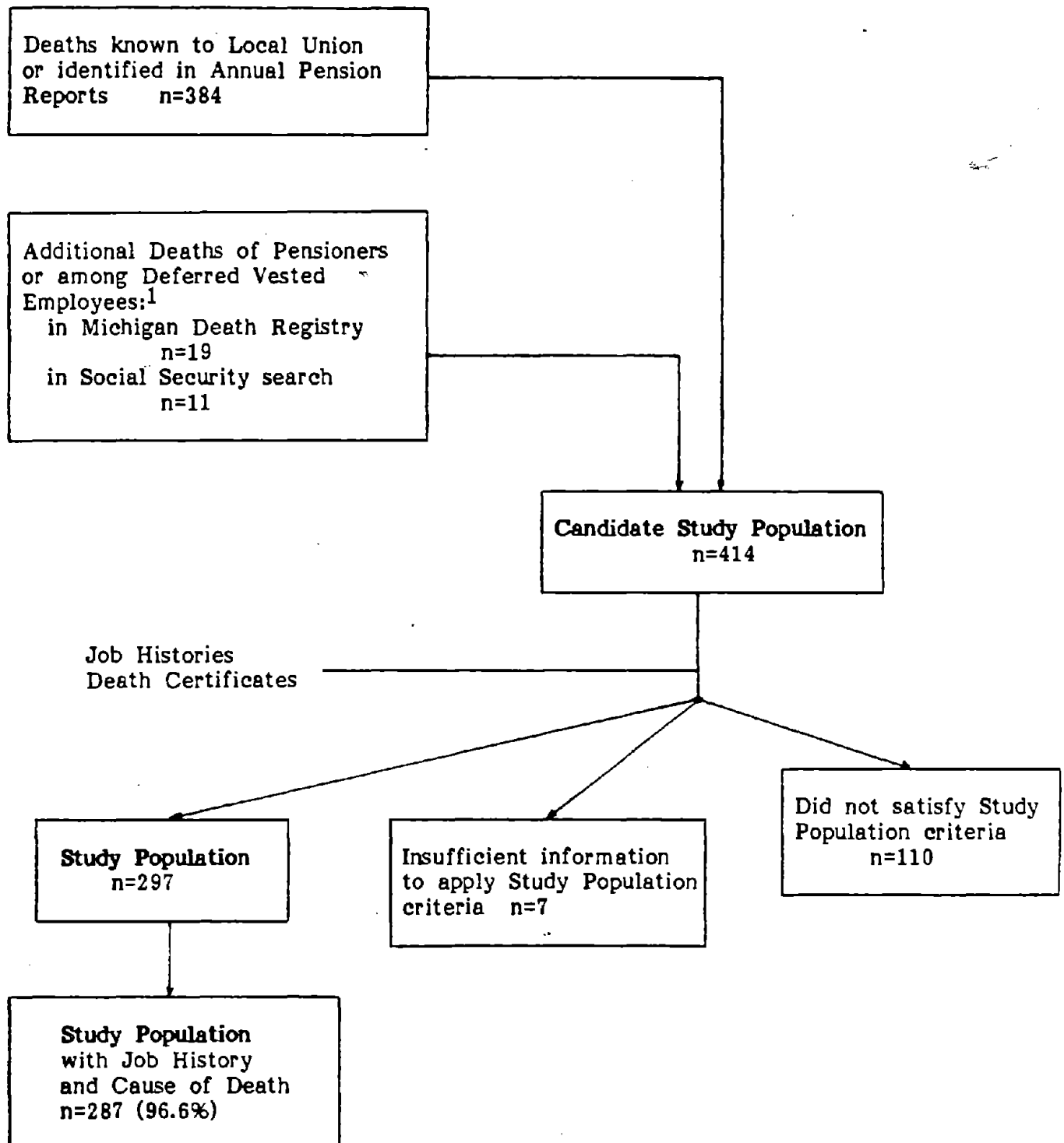
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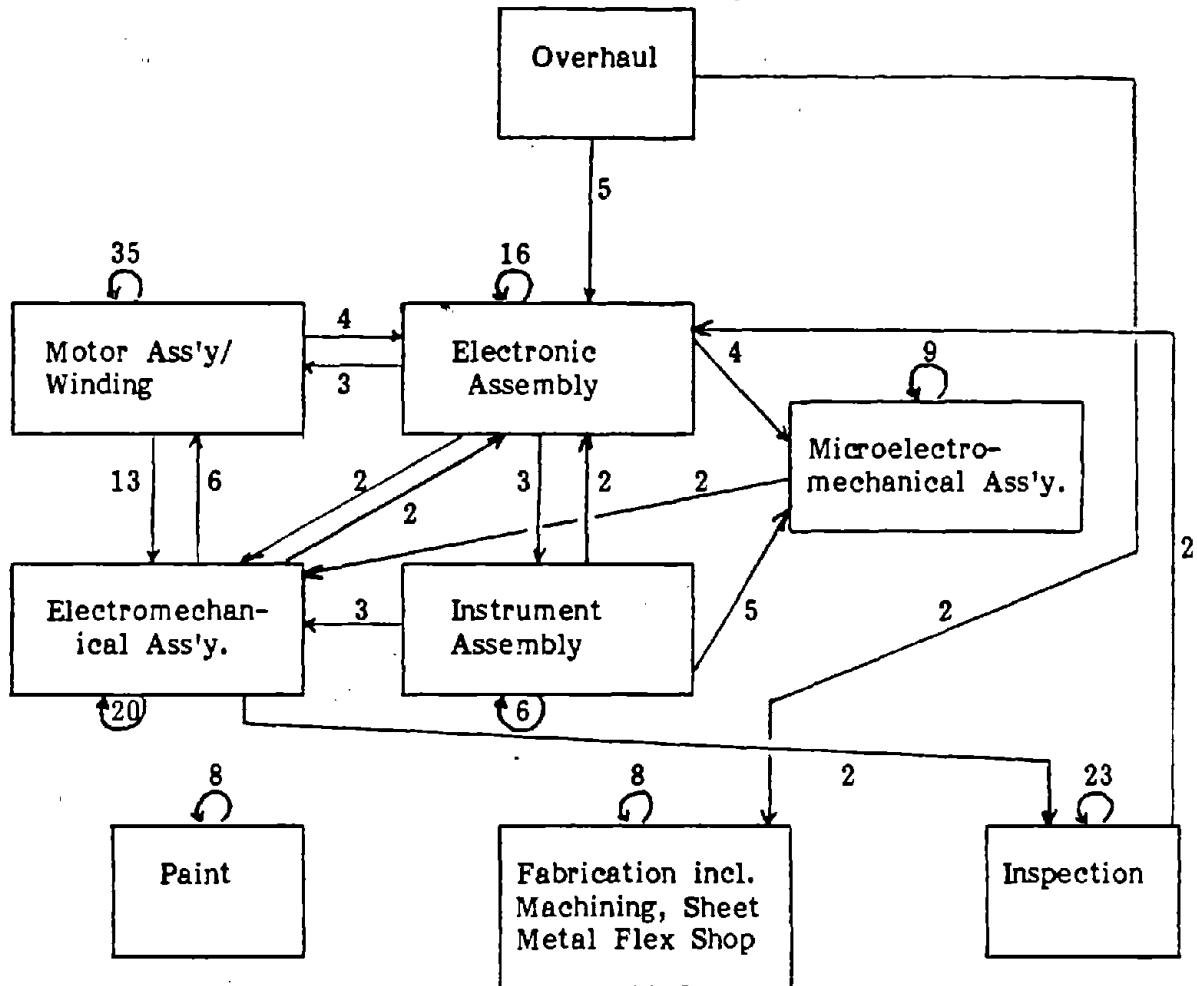
Figure 1
Derivation of Study Population



1. Employees who left employment after more than 10 yr's service but prior to retirement thus entitled to future pension.

Figure 2

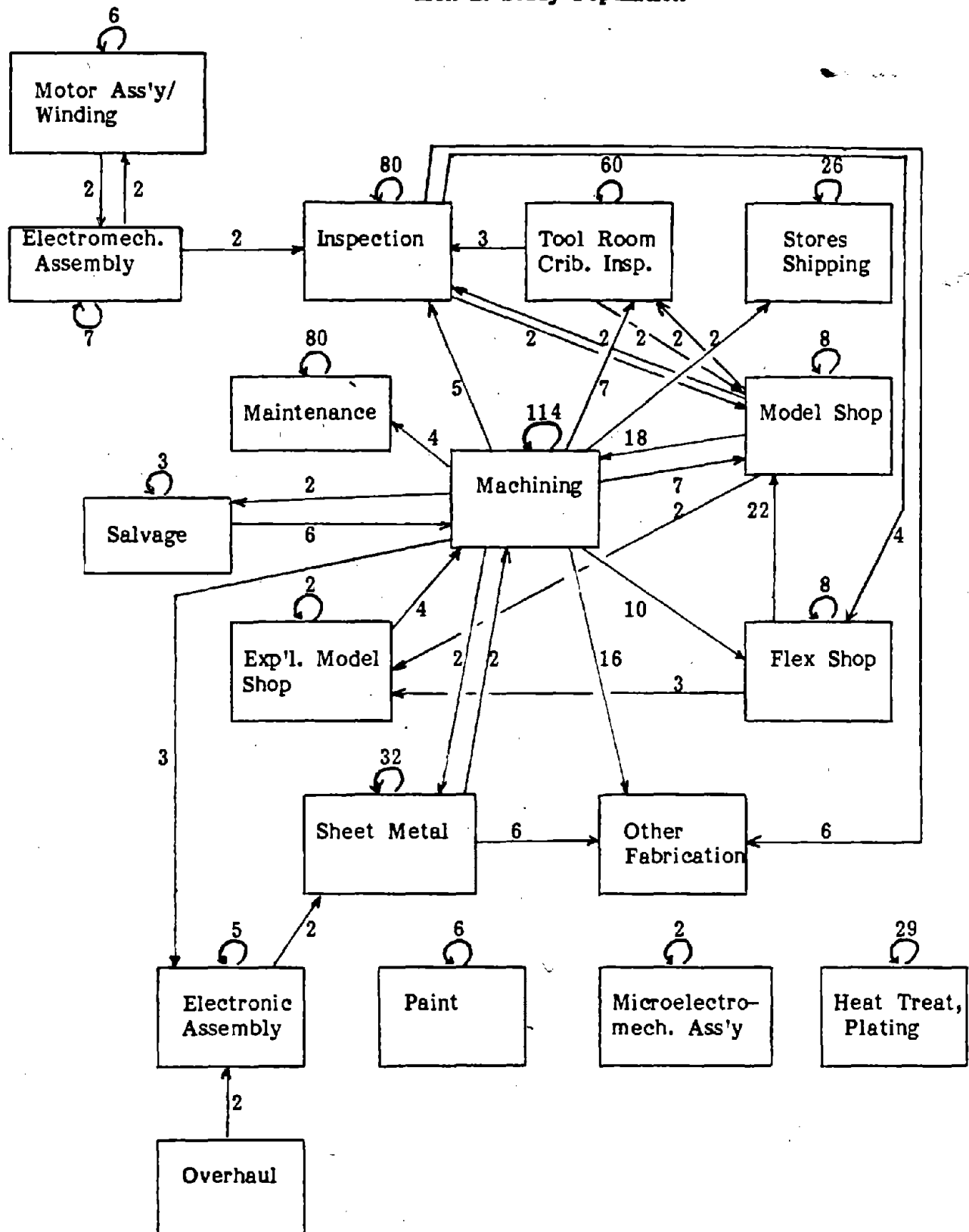
**Migration between Departmental Groups:
Women in Study Population**



1. Only pathways with 2 or more transfers are shown.
2. Based on departments indicated by consecutive seniority list matches to study population.

Figure 3

Migration Between Departmental Groups:
Men in Study Population



1. Only pathways with 2 or more transfers are shown.
2. Based on departments indicated by consecutive seniority list matches.

Table 1
Departmental Groups Used in Analysis

Dept. Grp. No.	Title
9	Packing
10	Receiving
11	Shipping
12	Stores
15	Incoming inspection
16	Parts inspection
21	Maintenance
30	Tool crib
33	Tool room
34	Tool room inspection
36	Flex shop inspection
37	Salvage
38	Electromechanical assembly inspection
39	Electronic inspection
40	Plating & heat treating
41	Paint shop
42	Flex shop
43	Sheet metal
44	Machine shop
45	Motor assembly
46	Electromechanical assembly
47	Electronic assembly
48	Instrument assembly
49	Operation pull-out
50	Overhaul inspection
53	Test equipment and test equipment inspection
54	Parts cleaning
55	Production control
56	Inspection, test
57	Other fabrication (excludes machining, sheet metal)
58	Microelectronic assembly
63	Winding section inspection
64	Instrument inspection
65	Winding section
76	Model shop (hanger)
77	Model shop inspection (hanger)
79	Experimental model shop
80	Experimental model shop inspection

1. Groupings of specific departments identified on the five seniority lists used to construct work histories.

Table 2
Selected Values of Weighting Function Used in
Calculation of Cumulative Exposures

Weighting Function	Time of Exposure (t) in Years Prior to Death ²								
	30	25	20	15	12.5	10	7.5	5	2.5
w(t) ¹	.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 3

**Distribution of Study Population by
Age at Death and Year of Death¹**

White Men		Year of Death						
		1955 ² -	1960-	1965-	1970-	1975-	1980 ³ -	All Years
Age at Death								
40		0	0	1	1	0	0	2
40-		0	0	1	2	2	1	6
50-		0	1	9	11	12	9	42
60-		0	4	9	23	20	21	77
70-		0	3	9	19	20	15	66
80-		0	0	0	2	7	6	15
90-		0	0	0	0	0	2	2
All Ages		0	8	29	58	61	54	Total 210

White Women		Year of Death						
		1955 ² -	1960-	1965-	1970-	1975-	1980 ³ -	All Years
Age at Death								
40		0	0	0	0	0	0	0
40-		0	0	2	2	4	0	8
50-		0	0	2	6	7	4	19
60-		1	1	3	4	4	7	20
70-		0	1	2	4	3	5	15
80-		0	1	1	4	3	1	10
90-		0	0	0	1	0	2	3
All Ages		1	3	10	21	21	19	Total 75

1. Study population with job history and cause of death information (not including 2 non-white decedents).
2. 1958-1959 (2-year period)
3. 1980-1983 (4-year period)

Table 4

**Distribution of White Men on Dates of Hire, Termination
and Death in Selected Departments of Longest Duration¹**

Department	Date of Hire					Date of Termination					Date of Death					Total		
	1940-	45-	50-	55-	60+	1955-	60-	65-	70-	75-	80+	1955-	60-	65-	70-		75-	80+
Machining	n	3	24	25	4		1	10	17	15	11	2	4	5	16	19	12	56
	%	5.4	43.	45.	7.1		1.8	18.	30.	27.	20.	3.6	7.1	8.9	29.	34.	21.	
Fabrication ²	n	2	6	8	1	1		6	3	7	2			4	4	7	3	18
	%	11.	33.	44.	5.6	5.6		33.	17.	39.	11.			22.	22.	39.	17.	
Inspection	n	3	12	14	1		7	7	8	8	4	4	5	7	9	9	9	39
	%	10.	40.	47.	3.3		23.	23.	27.	13.	13.	4	17.	23.	30.	30.	30.	
All Assembly	n	3	5	4	5		2	2	6	3	3	1	2	2	5	4	6	17
	%	18.	29.	23.	29.		12.	12.	35.	18.	18.	5.9	6.3	12.	29.	23.	35.	
Maintenance	n	6	7	12	7		3	11	8	5	2	3	2	2	9	8	11	32
	%	19.	22.	38.	22.		9.4	34.	25.	16.	6.3	9.4	6.3	6.3	28.	25.	34	
All Depart- ments	n	25	74	90	20	1	13	44	63	48	29	13	8	29	58	61	54	210
	%	12.	35.	43.	9.5	.48	6.2	21.	30.	23.	14.	6.2	3.8	14.	28.	29.	26.	

1. Department of Longest Duration: the departmental grouping in which a worker had the greatest weighted cumulative duration (weighted to account for latency; see Methods).

2. Fabrication: includes all fabrication departments except machining.

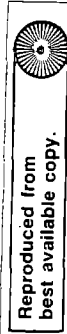


Table 5

Distribution of White Women on Dates of Hire, Termination
and Death in Selected Departments of Longest Duration¹

Department	Date of Hire		Date of Termination					Date of Death					Total				
	1940-	45-	50-	55-	60+	1955-	60-	65-	70-	75-	80+	1955-		60-	65-	70-	75-
Motor Ass'y & Winding	n	14	4	7		6	7	8	3	1		1	2	9	8	5	25
	%	56.	16.	28.		24.	28.	32.	12.	4.0		4.0	8.0	36.	32.	20.	
E.M., Micro- E.M., Instr. ²	n	9		8	3	4	3	7		4	2	2	3	6	5	4	20
	%	45.		40.	15.	20.	15.	35.		20.	10.	10.	15.	30.	25.	20.	
Electronic Ass'y.	n	3	1	4	3	2	2	2	2	2	3	1	1	3	3	4	11
	%	27.	9.1	36.	27.	18.	18.	18.	18.	18.	27.	9.1	14.	27.	27.	36.	
Inspection	n	5	1	1		1	4			1	1	1	1	2	2	2	7
	%	71.	14.	14.		14.	57.			14.	14.	14.	14.	29.	29.	29.	
Paint	n	6				3	2	1				1	2	1		2	6
	%	100.				50.	33.	17.				17.	33.	17.		33.	
All Depart- ments	n	38	6	24	7	14	14	24	7	9	7	1	3	10	21	19	75
	%	51.	8.0	32.	9.3	19.	19.	32.	9.3	12.	9.3	1.3	4.0	13.	28.	28.	25.

1. Department of Longest Duration: the departmental grouping in which a worker had the greatest weighted cumulative duration (weighted to account for latency; see Methods).

2. E.M. - Electromechanical Assembly.

Table 6

**Mean Cumulative Durations in Departmental Groupings,
Ranked for White Men and Women of Study Population¹**

White Men			White Women		
Departmental Group	$\bar{X}(2)$	$N_x(3)$	Departmental Group	$\bar{X}$	N_x
Machining	31.7	79	All Assembly ⁵	107.	62
Maintenance	20.6	38	Electromech. Ass'y.	27.4	29
Inspection	20.3	44	Motor Ass'y.	24.9	22
Fabrication ⁴	18.6	65	Electronic Ass'y.	19.4	22
Tool Rm./Crib	13.8	34	Winding	19.2	19
All Assembly ⁵	10.5	35	Inspection	19.1	10
Stores	6.25	16	Micro-E.M. Ass'y.	8.27	13
Electronic Ass'y.	3.21	17	Instrument Ass'y.	7.75	14
Electromech. Ass'y.	3.00	9	Fabrication ⁴	4.40	4
Motor Ass'y.	1.49	5	Machining	1.40	2
Winding	1.37	6			
Instrument Ass'y.	.733	4			
Micro-E.M. Ass'y.	.686	5			
All Departments	148.	210	All Departments	153.	75

1. Weighted cumulative duration, in months; weighted to account for latency of mortality in relation to exposures (see Methods).
2. Mean calculated over entire subpopulation (e.g. white men).
3. Number in subpopulation with cumulative exposure 1 or more months (i.e. "ever-exposed").
4. Fabrication: includes all fabrication departments except machining departments.
5. All Assembly: includes electronic, electro-mechanical, motor, instrument, micro-electromechanical assembly departments, and winding department.

Table 7

Mean Cumulative Durations in Departmental Groupings,
Weighted to Emphasize the Period Prior to 1960,
Ranked for White Men and Women of Study Population¹

White Men			White Women		
Departmental Group	$\bar{X}(2)$	$N_x(3)$	Departmental Group	$\bar{X}$	N_x
Machining	19.3	76	All Assembly ⁵	69.4	62
Maintenance	11.5	32	Motor Ass'y.	24.2	22
Inspection	10.9	43	Electromech. Ass'y.	18.9	25
Fabrication ⁴	10.2	42	Inspection	11.4	10
Tool Rm/Crib	8.89	31	Winding	10.9	19
All Assembly ⁵	5.14	28	Electronic Ass'y.	9.09	18
Stores	3.98	12	Instrument Ass'y	5.49	12
Electromech. Ass'y.	2.25	9	Fabrication	2.59	2
Motor Ass'y.	1.44	5	Machining	0.85	2
Electronic Ass'y.	0.67	11	Micro-E.M. Ass'y.	0.81	11
Instrument Ass'y.	0.45	4			
Winding	0.28	5			
Micro-E.M. Ass'y.	.048	2			
All Departments ⁶	148.	210	All Departments	153.	75

1. Weighted cumulative duration, in months; weighted both to account for latency of mortality in relation to exposures, and to emphasize exposures prior to 1960.
2. Mean calculated over entire subpopulation (e.g. white men).
3. Number in subpopulation with cumulative exposure 1 or more months (i.e. "ever-exposed").
4. Fabrication: includes all fabrication departments except machining departments.
5. All Assembly: includes electronic, electro-mechanical, motor, instrument, micro-electromechanical assembly departments, and winding department.
6. Weighted durations but not emphasizing period prior to 1960.

Table 8

Distribution of Study Population on Cumulative
Exposure Measures for Five Categories of Exposure

		Cumulative Exposure ¹							
		0	1-49	50-99	100-199	200-399	400-799	800+	Mean ⁴
<u>White Men (n=210)</u>									
Solvents	n	42	31	38	47	42	10		125.
	%	20.	15.	18.	22.	20.	4.8		
Epoxies ² ...	n	133	62	7	4	4			14.1
	%	63.	30.	3.3	1.9	1.9			
Cyano- acrylates ³ ...	n	153	29	23	5				13.0
	%	73.	14.	11.	2.4				
Solder/ Flux	n	152	35	14	8	1			15.2
	%	72.	17.	6.7	3.8	0.5			
Cutting Fluids	n	100	17	17	32	33	9	2	107.
	%	48.	8.1	8.1	15.	16.	4.3	1.0	
<u>White Women (n=75)</u>									
Solvents	n	6	4	12	28	20	5		169.
	%	8.0	5.3	16.	37.	27.	6.7		
Epoxies ² ...	n	8	6	5	28	15	13		203.
	%	11.	8.0	6.7	37.	20.	17.		
Cyano- acrylates ³ ...	n	24	13	7	11	13	7		129.
	%	32.	17.	9.3	15.	17.	9.3		
Solder/ Flux	n	35	7	19	7	2	4	1	82.8
	%	47.	9.3	25.	9.3	2.7	5.3	1.3	
Cutting Fluids	n	67	5	1	1	1			6.53
	%	89.	6.7	1.3	1.3	1.3			

1. Cumulative exposures, in exposure-months, weighted both to account for latency of death and to emphasize exposures prior to 1960; exposures assigned levels of 0,1,2,4 or 8 (see Methods).
2. Epoxies...: a broad category including not just epoxy resin systems but other materials used for analogous purposes, usually slow-curing.
3. Cyanoacrylates...: a broad category including not just cyanoacrylates but other adhesive systems and sealers (elastomers, etc.), usually fast-curing.
4. Mean exposure-months, calculated over entire subpopulation.

Table 9

Standardized Proportional Mortality Ratios for Selected Causes of Death in All White Men of Study Population

CAUSE OF DEATH	OBS	EXP	PMR	95% CI	CHI SQ	P
TOTAL DEATHS	210					
ALL MALIGNANT NEOPLASMS	43	47.40	0.91	0.70, 1.18	0.53	
CANCER OF DIGESTIVE ORGANS AND PERITONEUM	15	12.68	1.18	0.72, 1.93		
CANCER OF ESOPHAGUS	0	1.13	0.00	0.00, 2.65	0.45	
CANCER OF STOMACH	3	2.04	1.47	0.30, 4.30		
CANCER OF LARGE INTESTINE	4	4.43	0.90	0.25, 2.31		
CANCER OF RECTUM	1	1.30	0.77	0.02, 4.27		
ALL CANCER OF LIVER - PRIMARY ONLY	0	0.88	0.00	0.00, 3.40		
CANCER OF PANCREAS	7	2.58	2.71	1.09, 5.59		
ALL CANCER OF LUNG - PRIMARY AND SECONDARY	13	16.59	0.78	0.47, 1.32		
CANCER OF SKIN	0	0.72	0.00	0.00, 4.16		
CANCER OF PROSTATE	1	3.69	0.27	0.01, 1.51	0.85	
CANCER OF TESTIS	0	0.11	0.00	0.00, 27.24		
CANCER OF BLADDER	2	1.49	1.34	0.16, 4.85		
CANCER OF KIDNEY	2	1.15	1.74	0.21, 6.28		
CANCER OF BRAIN AND OTHER CENTRAL NERVOUS SYSTEM	0	1.10	0.00	0.00, 2.72		
ALL LYMPHOPOIETIC CANCER	7	4.06	1.72	0.69, 3.55		
ALL LYMPHOSARCOMA AND RETICULOSARCOMA	1	0.77	1.29	0.03, 7.22		
LEUKEMIA	3	1.54	1.95	0.40, 5.70		
CANCER OF OTHER LYMPHATIC TISSUE	2	1.29	1.55	0.19, 5.60		
ALLERGIC, ENDOCRINE, METABOLIC, NUTRITIONAL DIS.	1	3.71	0.27	0.01, 1.50		
ALL DISEASES OF NERVOUS SYSTEM AND SENSE ORGANS	3	1.69	1.78	0.37, 5.19		
ARTERIOSCLEROTIC HEART DISEASE, INCLUDING CHD	94	79.34	1.18	1.01, 1.39	4.38	
ALL VASCULAR LESIONS OF CNS	14	14.81	0.95	0.57, 1.56	0.05	
ALL RESPIRATORY DISEASES	12	14.79	0.81	0.47, 1.40	0.57	
ALL PNEUMONIA	5	4.58	1.09	0.35, 2.55		
EMPHYSEMA	4	3.66	1.09	0.30, 2.80		
ASTHMA	0	0.26	0.00	0.00, 11.52		
ALL DISEASES OF DIGESTIVE SYSTEM	9	9.09	0.99	0.52, 1.87	0.0	
ALL GASTRIC AND DUODENAL ULCER	0	1.07	0.00	0.00, 2.80		
CIRRHOSIS OF LIVER	5	4.65	1.08	0.35, 2.51		
CHRONIC NEPHRITIS	0	0.48	0.00	0.00, 6.24		
ALL ACCIDENTS	5	7.14	0.70	0.30, 1.63	0.68	
SUICIDE	2	2.79	0.72	0.09, 2.59		

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

Table 10

Standardized Proportional Mortality Ratios for Selected Causes of Death
in All White Women of Study Population

CAUSE OF DEATH	OBS	EXP	PMR	95% CI	CHI SQ	P
TOTAL DEATHS	75					
ALL MALIGNANT NEOPLASMS	36	21.91	1.64	1.26, 2.14	13.69	<.001
CANCER OF DIGESTIVE ORGANS AND PERITONEUM	13	5.27	2.47	1.49, 4.09	12.26	<.001
CANCER OF ESOPHAGUS	0	0.20	0.00	0.00, 14.98		
CANCER OF STOMACH	3	0.63	4.79	0.98, 13.92		.052
CANCER OF LARGE INTESTINE	6	2.32	2.59	0.95, 5.63		.062
CANCER OF RECTUM	0	0.50	0.00	0.00, 5.99		
ALL CANCER OF LIVER - PRIMARY ONLY	0	0.47	0.00	0.00, 6.37		
CANCER OF PANCREAS	4	1.00	4.01	1.09, 10.23		.038
ALL CANCER OF LUNG - PRIMARY AND SECONDARY	3	3.08	0.97	0.20, 2.85		
CANCER OF SKIN	0	0.29	0.00	0.00, 10.33		
CANCER OF BREAST	4	5.04	0.79	0.31, 2.01	0.24	.003
CANCER OF ALL GENITAL ORGANS	10	3.19	3.14	1.51, 5.76		
CANCER OF ALL UTERUS	3	1.48	2.03	0.42, 5.93		.004
CANCER OF OTHER GENITAL ORGANS (2)	7	1.69	4.14	1.66, 8.54		
CANCER OF BLADDER	0	0.25	0.00	0.00, 11.98		
CANCER OF KIDNEY	1	0.34	2.90	0.07, 16.34		
CANCER OF BRAIN AND OTHER CENTRAL NERVOUS SYSTEM	1	0.54	1.85	0.05, 10.29		
ALL LYMPHOPOIETIC CANCER	4	1.73	2.31	0.63, 5.91		
LYMPHOSARCOMA AND RETICULOSARCOMA	2	0.37	5.43	0.65, 19.51		
LEUKEMIA	1	0.60	1.67	0.04, 9.26		
CANCER OF OTHER LYMPHATIC TISSUE	1	0.57	1.75	0.04, 9.75		
ALLERGIC, ENDOCRINE, METABOLIC, NUTRITIONAL DIS.	4	2.25	1.78	0.48, 4.55		
ALL DISEASES OF NERVOUS SYSTEM AND SENSE ORGANS	0	0.82	0.00	0.00, 3.65		
ARTERIOSCLEROTIC HEART DISEASE, INCLUDING CHD	15	20.34	0.74	0.49, 1.12	2.03	
ALL VASCULAR LESIONS OF CNS	5	7.44	0.67	0.30, 1.52	0.91	
ALL RESPIRATORY DISEASES	4	3.54	1.13	0.31, 2.89		
ALL PNEUMONIA	3	1.53	1.96	0.40, 5.73		
EMPHYSEMA	0	0.46	0.00	0.00, 6.51		
ASTHMA	0	0.16	0.00	0.00, 18.72		
ALL DISEASES OF DIGESTIVE SYSTEM	1	3.54	0.28	0.01, 1.57		
ALL GASTRIC AND DUODENAL ULCER	0	0.27	0.00	0.00, 11.10		
CIRRHOSIS OF LIVER	0	1.76	0.00	0.00, 1.70		
CHRONIC NEPHRITIS	0	0.21	0.00	0.00, 14.27		
ALL ACCIDENTS	2	2.31	0.86	0.10, 3.13		

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.

2. Cancer of Other Genital Organs (ICD-8: 183.0-184.9); all observed were ICD-8: 183 - ovary.

Table 11

**Standardized Proportional Mortality Ratios for Key
Causes of Death, in 5-Year Intervals**

White Women		Year of Death ¹				
Cancer of Ovary		1960-64	1965-69	1970-74	1975-79	1980-83
Obs.	0	1	3	3	0	
Exp.	.031	.211	.462	.584	.388	
SPMR	0.0	4.75	6.50	5.14	0.0	
Cancer of Colon						
Obs.	0	1	2	3	0	
Exp.	.081	.290	.628	.667	.620	
SPMR	0.0	3.45	3.19	4.50	0.0	
Cancer of Pancreas						
Obs.	0	0	3	0	1	
Exp.	.031	.114	.262	.286	.292	
SPMR	0.0	0.0	11.5	0.0	3.43	
Cancer of Stomach ²						
Obs.	0	0	1	1	0	
Exp.	.036	.093	.176	.161	.146	
SPMR	0.0	0.0	5.68	6.21	0.0	
All Cancers						
Obs.	0	5	14	11	5	
Exp.	.524	2.65	5.74	7.15	5.62	
SPMR	0.0	1.89	2.44	1.54	0.89	
White Men						
Cancer of Pancreas						
Obs.	0	0	4	3	0	
Exp.	0.093	.343	.700	.766	.680	
SPMR	0.0	0.0	5.71	3.92	0.0	
All Cancers						
Obs.	3	3	11	16	10	
Exp.	1.54	5.77	12.3	14.3	13.4	
SPMR	1.95	0.52	0.89	1.12	0.75	

1. In 5-year intervals except for 1980-83: 4 years.
2. There was one death prior to 1960 (1959); this death was due to stomach cancer in a white woman.

Table 12

Standardized Proportional Mortality Ratios for Selected Causes of Death in Men Exposed to Epoxy-like Materials, pre-1960(1)

CAUSE OF DEATH	OBS	EXP	PMR	95% CI	CHI SQ	P
TOTAL DEATHS	77					
ALL MALIGNANT NEOPLASMS	17	17.94	0.95	0.63, 1.43	0.06	
CANCER OF DIGESTIVE ORGANS AND PERITONEUM	6	4.67	1.29	0.47, 2.80		
CANCER OF ESOPHAGUS	0	0.43	0.00	0.00, 6.97		
CANCER OF STOMACH	0	0.72	0.00	0.00, 4.16		
CANCER OF LARGE INTESTINE	1	1.66	0.60	0.02, 3.35		
CANCER OF RECTUM	0	0.46	0.00	0.00, 6.51		
ALL CANCER OF LIVER - PRIMARY ONLY	0	0.33	0.00	0.00, 9.08		
CANCER OF PANCREAS	5	0.97	5.18	1.67, 12.04		.006
ALL CANCER OF LUNG - PRIMARY AND SECONDARY	5	6.43	0.78	0.34, 1.79	0.35	
CANCER OF SKIN	0	0.29	0.00	0.00, 10.33		
CANCER OF PROSTATE	1	1.32	0.76	0.02, 4.21		
CANCER OF TESTIS	0	0.05	0.00	0.00, 59.92		
CANCER OF BLADDER	1	0.53	1.87	0.05, 10.48		
CANCER OF KIDNEY	0	0.45	0.00	0.00, 6.66		
CANCER OF BRAIN AND OTHER CENTRAL NERVOUS SYSTEM	2	1.56	1.29	0.16, 4.63		
ALL LYMPHOPLASTIC CANCER	0	0.29	0.00	0.00, 10.33		
LYMPHOSARCOMA AND RETICULOSARCOMA	1	0.57	1.76	0.04, 9.75		
LEUKEMIA	1	0.51	1.98	0.05, 10.89		
CANCER OF OTHER LYMPHATIC TISSUE	1	1.36	0.73	0.02, 4.08		
ALLERGIC, ENDOCRINE, METABOLIC, NUTRITIONAL DIS.	1	0.67	1.50	0.04, 8.29		
ALL DISEASES OF NERVOUS SYSTEM AND SENSE ORGANS	37	28.34	1.31	1.01, 1.68	4.22	.05
ARTERIOSCLEROTIC HEART DISEASE, INCLUDING CHD	4	5.00	0.80	0.31, 2.05	0.22	
ALL VASCULAR LESIONS OF CNS	4	5.34	0.75	0.29, 1.91	0.37	
ALL RESPIRATORY DISEASES	2	1.56	1.29	0.16, 4.63		
ALL PNEUMONIA	0	1.24	0.00	0.00, 2.42		
EMPHYSEMA	0	0.09	0.00	0.00, 33.29		
ASTHMA	3	3.44	0.87	0.18, 2.55		
ALL DISEASES OF DIGESTIVE SYSTEM	0	0.36	0.00	0.00, 8.32		
ALL GASTRIC AND DUODENAL ULCER	2	1.85	1.08	0.13, 3.90		
CIRRHOSIS OF LIVER	0	0.16	0.00	0.00, 18.72		
CHRONIC NEPHRITIS	2	2.97	0.67	0.08, 2.43		
ALL ACCIDENTS	0	1.18	0.00	0.00, 2.54		
SUICIDE	0					

1. All white men with 1 or more exposure-months in jobs using epoxy-like materials, durations weighted to account for latency and to emphasize pre-1960 exposures.

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

Table 13

Standardized Proportional Mortality Ratios for Selected Causes of Death in Women in Motor Assembly and Winding Departments(1)

CAUSE OF DEATH	OBS	EXP	PMR	95% CI	(2) CHI SO	(2) P
TOTAL DEATHS	26					
ALL MALIGNANT NEOPLASMS	12	6.88	1.74	1.10, 2.77	5.55	.02
CANCER OF DIGESTIVE ORGANS AND PERITONEUM	6	1.80	3.34	1.22, 7.26		.021
CANCER OF ESOPHAGUS	0	0.07	0.00	0.00, 42.80		
CANCER OF STOMACH	2	0.22	9.29	1.10, 32.82		.042
CANCER OF LARGE INTESTINE	2	0.79	2.52	0.31, 9.14		
CANCER OF RECTUM	0	0.17	0.00	0.00, 17.62		
ALL CANCER OF LIVER - PRIMARY ONLY	0	0.16	0.00	0.00, 18.72		
CANCER OF PANCREAS	2	0.34	5.92	0.71, 21.24		.092
ALL CANCER OF LUNG - PRIMARY AND SECONDARY	2	0.89	2.25	0.27, 8.11		
CANCER OF SKIN	0	0.08	0.00	0.00, 37.45		
CANCER OF BREAST	1	1.47	0.68	0.02, 3.78		
CANCER OF ALL GENITAL ORGANS	2	0.99	2.02	0.24, 7.29		
CANCER OF ALL UTERUS	0	0.46	0.00	0.00, 6.51		
CANCER OF OTHER GENITAL ORGANS (3)	2	0.52	3.83	0.47, 13.89		
CANCER OF BLADDER	0	0.09	0.00	0.00, 33.29		
CANCER OF KIDNEY	0	0.11	0.00	0.00, 27.24		
CANCER OF BRAIN AND OTHER CENTRAL NERVOUS SYSTEM	1	0.16	6.23	0.16, 34.72		
ALL LYMPHOPOIETIC CANCER	0	0.56	0.00	0.00, 5.35		
LYMPHOSARCOMA AND RETICULOSARCOMA	0	0.12	0.00	0.00, 24.97		
LEUKEMIA	0	0.20	0.00	0.00, 14.98		
CANCER OF OTHER LYMPHATIC TISSUE	0	0.19	0.00	0.00, 15.77		
ALLERGIC, ENDOCRINE, METABOLIC, NUTRITIONAL DIS.	1	0.79	1.26	0.03, 7.03		
ALL DISEASES OF NERVOUS SYSTEM AND SENSE ORGANS	0	0.26	0.00	0.00, 11.52		
ARTERIOSCLEROTIC HEART DISEASE, INCLUDING CHD	8	7.91	1.01	0.58, 1.78	0.0	
ALL VASCULAR LESIONS OF CNS	2	2.87	0.70	0.08, 2.52		
ALL RESPIRATORY DISEASES	1	1.26	0.80	0.02, 4.41		
ALL PNEUMONIA	1	0.58	1.73	0.04, 9.58		
EMPHYSEMA	0	0.16	0.00	0.00, 18.72		
ASTHMA	0	0.05	0.00	0.00, 59.92		
ALL DISEASES OF DIGESTIVE SYSTEM	1	1.11	0.90	0.02, 5.01		
ALL GASTRIC AND DUODENAL ULCER	0	0.09	0.00	0.00, 33.29		
CIRRHOSIS OF LIVER	0	0.49	0.00	0.00, 6.11		
CHRONIC NEPHRITIS	0	0.08	0.00	0.00, 37.45		
ALL ACCIDENTS	0	0.70	0.00	0.00, 4.28		

1. All white women with 40 or more months duration in motor assembly or winding departments, durations weighted to account for latency and to emphasize pre-1960 exposures.

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

3. Cancer of Other Genital Organs (ICD-8: 183.0-184.9); all observed were ICD-8: 183 - ovary.

Table 14

**Standardized Proportional Mortality Ratios for Selected Causes of Death
In Women Exposed to Epoxy-like Materials, pre-1960(1)**

CAUSE OF DEATH	OBS	EXP	PMR	95% CI	(2)	CHI SQ	P
TOTAL DEATHS	28						
ALL MALIGNANT NEOPLASMS	11	6.83	1.61	0.99, 2.62		3.65	.06
CANCER OF DIGESTIVE ORGANS AND PERITONEUM	7	1.85	3.79	1.52, 7.80			.006
CANCER OF ESOPHAGUS	0	0.07	0.00	0.00, 42.80			
CANCER OF STOMACH	1	0.22	4.52	0.11, 25.25			
CANCER OF LARGE INTESTINE	5	0.82	6.08	1.97, 14.25			.003
CANCER OF RECTUM	0	0.17	0.00	0.00, 17.62			
ALL CANCER OF LIVER - PRIMARY ONLY	0	0.16	0.00	0.00, 18.72			
CANCER OF PANCREAS	1	0.35	2.88	0.07, 15.87			
ALL CANCER OF LUNG - PRIMARY AND SECONDARY	2	0.91	2.21	0.27, 7.93			
CANCER OF SKIN	0	0.08	0.00	0.00, 37.45			
CANCER OF BREAST	0	1.42	0.00	0.00, 2.11			
CANCER OF ALL GENITAL ORGANS	2	0.93	2.15	0.26, 7.76			
CANCER OF ALL UTERUS	1	0.42	2.38	0.06, 13.23			
CANCER OF OTHER GENITAL ORGANS (3)	1	0.50	1.99	0.05, 11.11			
CANCER OF BLADDER	0	0.10	0.00	0.00, 29.96			
CANCER OF KIDNEY	0	0.11	0.00	0.00, 27.24			
CANCER OF BRAIN AND OTHER CENTRAL NERVOUS SYSTEM	0	0.15	0.00	0.00, 19.97			
ALL LYMPHOPOIETIC CANCER	0	0.57	0.00	0.00, 5.26			
LYMPHOSARCOMA AND RETICULOSARCOMA	0	0.11	0.00	0.00, 27.24			
LEUKEMIA	0	0.20	0.00	0.00, 14.98			
CANCER OF OTHER LYMPHATIC TISSUE	0	0.20	0.00	0.00, 14.98			
ALLERGIC, ENDOCRINE, METABOLIC, NUTRITIONAL DIS.	2	0.83	2.40	0.29, 8.70			
ALL DISEASES OF NERVOUS SYSTEM AND SENSE ORGANS	0	0.26	0.00	0.00, 11.52			
ARTERIOSCLEROTIC HEART DISEASE, INCLUDING CHD	6	8.90	0.67	0.35, 1.28		1.44	
ALL VASCULAR LESIONS OF CNS	2	3.32	0.60	0.07, 2.17			
ALL RESPIRATORY DISEASES	2	1.37	1.46	0.18, 5.27			
ALL PNEUMONIA	1	0.67	1.49	0.04, 8.29			
EMPHYSEMA	0	0.16	0.00	0.00, 18.72			
ASTHMA	0	0.04	0.00	0.00, 74.90			
ALL DISEASES OF DIGESTIVE SYSTEM	1	1.13	0.89	0.02, 4.92			
ALL GASTRIC AND DUODENAL ULCER	0	0.10	0.00	0.00, 29.96			
CIRRHOISIS OF LIVER	0	0.45	0.00	0.00, 6.66			
CHRONIC NEPHRITIS	0	0.07	0.00	0.00, 42.80			
ALL ACCIDENTS	1	0.70	1.43	0.04, 7.94			

1. All white women with 200 or more exposure-months in jobs using epoxy-like materials. durations weighted to account for latency and to emphasize pre-1960 exposures.

2. 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.

3. Cancer of Other Genital Organs (ICD-8: 183.0-184.9); all observed were ICD-8: 183 - ovary.

Table 15

**Standardized Proportional Mortality Ratios for Selected Causes of Death
In Women Exposed to Cyanoacrylate and Related Materials, pre-1960(1)**

CAUSE OF DEATH	OBS	EXP	PMR	95% CI	(2)	CHI SQ	P
TOTAL DEATHS	37	11.02	2.00	1.43, 2.78	16.68	<.001	
ALL MALIGNANT NEOPLASMS	22	11.02	2.00	1.43, 2.78	16.68	<.001	
CANCER OF DIGESTIVE ORGANS AND PERITONEUM	7	2.62	2.67	1.07, 5.51		.036	
CANCER OF ESOPHAGUS	0	0.10	0.00	0.00, 29.96			
CANCER OF STOMACH	2	0.31	6.37	0.78, 23.29		.078	
CANCER OF LARGE INTESTINE	2	1.15	1.74	0.21, 6.28			
CANCER OF RECTUM	0	0.25	0.00	0.00, 11.98			
ALL CANCER OF LIVER - PRIMARY ONLY	0	0.22	0.00	0.00, 13.62			
CANCER OF PANCREAS	3	0.49	6.08	1.26, 17.90		.027	
ALL CANCER OF LUNG - PRIMARY AND SECONDARY	2	1.53	1.31	0.16, 4.72			
CANCER OF SKIN	0	0.14	0.00	0.00, 21.40			
CANCER OF BREAST	2	2.55	0.78	0.09, 2.83			
CANCER OF ALL GENITAL ORGANS	6	1.64	3.66	1.34, 7.97		.014	
CANCER OF ALL UTERUS	2	0.76	2.62	0.32, 9.50		.023	
CANCER OF OTHER GENITAL ORGANS (3)	4	0.86	4.64	1.27, 11.90			
CANCER OF BLADDER	0	0.12	0.00	0.00, 24.97			
CANCER OF KIDNEY	1	0.17	5.79	0.15, 32.68			
CANCER OF BRAIN AND OTHER CENTRAL NERVOUS SYSTEM	1	0.28	3.61	0.09, 19.84			
ALL LYMPHOPOIETIC CANCER	3	0.86	3.48	0.72, 10.20			
ALL LYMPHOSARCOMA AND RETICULOSARCOMA	1	0.19	5.21	0.13, 29.24			
LEUKEMIA	1	0.30	3.33	0.08, 18.52			
CANCER OF OTHER LYMPHATIC TISSUE	1	0.28	3.62	0.09, 19.84			
ALLERGIC, ENDOCRINE, METABOLIC, NUTRITIONAL DIS.	0	1.11	0.00	0.00, 2.70			
ALL DISEASES OF NERVOUS SYSTEM AND SENSE ORGANS	0	0.39	0.00	0.00, 7.68			
ARTERIOSCLEROTIC HEART DISEASE, INCLUDING CHD	6	10.14	0.59	0.31, 1.14	2.47		
ALL VASCULAR LESIONS OF CNS	3	3.69	0.81	0.17, 2.38			
ALL RESPIRATORY DISEASES	1	1.72	0.58	0.01, 3.23			
ALL PNEUMONIA	1	0.75	1.33	0.03, 7.41			
EMPHYSEMA	0	0.24	0.00	0.00, 12.48			
ASTHMA	0	0.08	0.00	0.00, 37.45			
ALL DISEASES OF DIGESTIVE SYSTEM	1	1.76	0.57	0.01, 3.16			
ALL GASTRIC AND DUODENAL ULCER	0	0.14	0.00	0.00, 21.40			
CIRRHOSIS OF LIVER	0	0.90	0.00	0.00, 3.33			
CHRONIC NEPHRITIS	0	0.11	0.00	0.00, 27.24			
ALL ACCIDENTS	0	1.16	0.00	0.00, 2.58			

1. All white women with 60 or more exposure-months in jobs using cyanoacrylate and related materials, durations weighted to account for latency and to emphasize pre-1960 exposures.

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

3. Cancer of Other Genital Organs (ICD-8: 183.0-184.9); all observed were ICD-8: 183 - ovary.

Table 16

Summary of SPMR Findings in Exposure Groups¹

Exposure Group	n	All Cancer		Cancer of Pancreas		Cancer of Colon		Cancer of Stomach		Cancer of Ovary	
		OBS/EXP	PMR	OBS/EXP	PMR	OBS/EXP	PMR	OBS/EXP	PMR	OBS/EXP	PMR
Women											
Solvents	33	12/8.2	1.5	1/4.0	2.5	3/9.6	3.1	1/2.6	3.8	1/6.1	1.7
Epoxy-like	28	11/6.8	1.6	1/3.5	2.9	5/8.2	6.1	1/2.2	4.5	1/5.0	2.0
Cyanoacrylate-like	37	22/11.	2.0	3/4.9	6.1	2/1.2	1.7	2/3.1	6.4	4/8.6	4.6
Solder/Flux	33	19/11.	1.7	2/4.8	4.2	4/1.1	3.7	1/2.7	3.8	2/9.0	2.2
Motor/Wind Depts.	26	12/6.9	1.7	2/3.4	5.9	2/7.9	2.5	2/2.2	9.3	2/5.2	3.8
EM/Micro-EM Depts.	28	12/7.5	1.6	1/3.8	2.7	1/8.7	1.2	0/2.4	0.0	3/5.6	5.4
Inspection Depts.	9	6/2.6	2.3	1/1.2	8.2	1/2.8	3.6	0/0.7	0.0	3/2.0	15.
All	75	36/22.	1.6	4/1.0	4.0	6/2.3	2.6	3/6.3	4.8	7/1.7	4.1
Men											
Solvents	93	22/21.	1.0	3/1.1	2.6	3/2.0	1.5	1/9.1	1.1	—	—
Epoxy-like	77	17/18.	.95	5/9.7	5.2	1/1.7	0.6	0/7.2	0.0	—	—
Cutting Fluids	88	20/20.	.98	2/1.1	1.8	3/1.9	1.6	1/8.6	1.2	—	—
Machining Depts.	41	10/9.5	1.1	1/5.2	1.9	3/8.7	3.4	1/4.2	2.4	—	—
All	210	43/47.	.91	7/2.6	2.7	4/4.4	0.9	3/2.0	1.5	—	—

1. Exposure groups selected by specifying a minimum (latency-weighted) duration (for departments), or exposure-duration (for 5 exposure categories), emphasizing pre-1960 exposures. These exposure groups are not mutually exclusive.

Table 17

**Effects of Latency-Based Restriction of Study
Population and Latency-Weighting of Exposure Measures on SPMR Findings**

Exposure Group	n	All Cancer OBS/EXP	PMR	Cancer of Pancreas OBS/EXP	PMR	Colon Cancer OBS/EXP	PMR	Stomach Cancer OBS/EXP	PMR	Cancer of Ovary OBS/EXP	PMR
Women											
Study Population ¹	75	36/22.	1.6	4/1.0	4.0	6/2.3	2.6	3/.63	4.8	7/1.7	4.1
Extended Population ¹	81	40/24.	1.7	4/1.1	3.8	6/2.5	2.4	3/.68	4.4	7/1.9	3.7
Epoxy-like ²	28	11/6.8	1.6	1/35	2.9	5/.82	6.1	1/.22	4.5	1/.50	2.0
Epoxy-like, Extended ²	32	16/9.9.	1.6	1/.46	2.2	5/1.0	4.8	0/.21	0.0	2/.76	2.6
EM/Micro-EM. Depts. ³	28	12/7.5	1.6	1/38	2.7	1/.87	1.2	0/.24	0.0	3/.56	5.4
EM/Micro-EM, Extended ³	31	17/9.4	1.8	0/.40	0.0	2/.96	2.1	1/.26	3.9	2/.74	2.7
Men											
Study Population ¹	210	43/47	.91	7/2.6	2.7	4/4.4	.90	3/2.0	1.5	—	—
Extended Population ¹	252	51/56.	.92	8/3.1	2.6	5/5.1	.98	3/2.5	1.2	—	—
Epoxy-like ⁴	77	17/18.	.95	5/.97	5.2	1/1.7	.60	0/.72	0.0	—	—
Epoxy-like, Extended ⁴	82	19/19.	.98	5/1.0	4.8	1/1.8	.56	2/.77	2.6	—	—
Solvents ⁵	93	22/21.	1.0	3/1.1	2.6	3/2.0	1.5	1/.91	1.1	—	—
Solvents, Extended ⁵	103	21/24.	.87	4/1.3	3.1	3/2.3	1.3	1/.98	1.0	—	—

1. Study population: as defined in Methods using weighted cumulative duration of employment to account for latency; Extended population: study population plus those candidates excluded by latency-weighting requirement.
2. For study population: those with epoxy-like weighted exposure-months not less than 200; for Extended population: those with unweighted exposure-months not less than 540 and duration from hire until death not less than 20 years.
3. For study population: those with weighted duration in electromechanical (EM) departments not less than 6 mos.; Extended population: those with unweighted duration not less than 60 months and duration from hire until death not less than 20 years.
4. For study population: those with epoxy-like weighted exposure-months not less than 1; for Extended population, those with unweighted exposure-months not less than 1 and duration from hire until death not less than 20 years.
5. For study population: those with solvents weighted exposure-months not less than 120; for Extended population: those with unweighted exposure-months not less than 240 and duration from hire until death not less than 20 years.

Table 18

Crude Mortality Odds Ratios in Exposure Strata¹

<u>Exposure Strata</u>	<u>Colon Cancer in Women</u>			
Epoxy-like Materials (Exposure-months)	Cases	Controls ²	Odds	Odds Ratio ⁽³⁾
0	0	8	.058	1.0
1-199	1	38	.039	.67
200+	5	23	.234	4.0
Total	6	69	.087	

	<u>Cancer of Ovary in Women</u>			
Cyanoacrylate-like Materials (Exposure-months)	Cases	Controls ²	Odds	Odds Ratio
0	2	22	.091	1.0
1-199	2	29	.069	.76
200+	3	17	.176	1.9
Total	7	68	.103	

	<u>Cancer of Pancreas in Men</u>			
Epoxy-like Materials (Exposure-months)	Cases	Controls ²	Odds	Odds Ratio
0	2	131	.015	1.0
1-99	4	65	.062	4.0
100+	1	7	.143	9.4
Total	7	203	.034	

1. Potential confounding exists due to age, year of death and other exposures.
2. Controls: deaths due to all other causes.
3. 0.5 added to all cells because of 0 unexposed cases.

Table 19

**Logistic Regression Analyses of Association Between
Death Due to Colon Cancer and Exposures in
Electronics Production in Women (n=75)**

Model	Predictor ⁽¹⁾	Effect Estimate, SE	Removal from Model ⁽²⁾		Adj. OR ⁽³⁾	95% CI
			$\Delta(-2\ln L)$	P		
1. ⁽⁴⁾	Intercept Epoxy	-.380, .896 .00527, .00231	— 5.68	— .009	.68 3.54	1.24, 10.0
2.	Intercept (Epoxy) 0.5	-1.64, 1.46 .175, .080	— 5.89	— .008	.19 15.1	
3.	Intercept Epoxy, truncated ⁽⁵⁾	-1.70, 1.76 .017, .0096	— 3.81	— .03	.18 30.0	
4.	Intercept Cyanoacrylate	1.290, .542 -.00277, .00414	— .71	— —	3.63 .51	
5.	Intercept Solder/flux	.586, .519 .00333, .00251	— 3.64	— .03	1.80 2.22	
6.	Intercept Solvent	.296, .802 .00380, .00304	— 1.61	— .10	1.34 2.49	
7.	Intercept Epoxy Solder/flux	-.578, 1.20 .00489, .00291 .00267, .00467	— 3.98 1.94	— .02 .08	.56 3.23 1.90	
8.	Intercept Epoxy Electronics Ass'y	-.542, .996 .00505, .00260 .0148, .0185	— 5.20 1.68	— .01 .10	.58 3.36 2.43	
9.	Intercept Age at death	1.10, .561 -.0110, .044	— .082	— —	3.00 .89 (10-yr.)	

- Predictors are exposures (in exposure-months using latency-weighted durations and emphasizing pre-1960 exposures) or department durations (in months of latency-weighted duration, emphasizing the pre-1960 period) and age at death (years greater than age 55).
- Hypothesis testing consisted of removing a predictor from the model and assessing the change in $-2\ln(\text{likelihood})$, distributed as chi-squared; 1-tailed P-values were computed.
- The adj. OR for the intercept is the standardized mortality odds ratio estimated for the study population adjusting for the predictors in model, i.e., for the "unexposed." For exposure predictors, the adj. OR is the exposure odds ratio within the study population, standardized to the reference population and applied to 5 years (wt. duration) of exposure (and exposure level 4 where applicable). For age at death (model 9), the adj. OR is for a 10-yr. age increment. Confidence interval (95% CI) is based on chi-squared (test-based).

4. Final Model: $\ln\left(\frac{p}{1-p}\right) = -.38 + \ln\left(\frac{r}{1-r}\right) + .00527X$

where: p = probability that death was due to colon cancer;
r = age-, year-, race-, sex-specific proportional mortality rate for colon cancer in U.S.;
X = exposure to epoxy-like materials in exposure-months.

- Epoxy, truncated: all epoxy exposure values in excess of 200 exposure-months were set equal to 200.

Table 20

Logistic Regression Analysis of Association Between Death Due to Cancer of the Colon and Exposure to Epoxy-like Materials in Women: Goodness of Fit

Epoxy-like Exposure Strata (exposure-months)	n	Cases of Colon Cancer				
		Predicted ⁽¹⁾	Observed	Expected ⁽²⁾	r, mean ⁽²⁾	Pred. OR ⁽³⁾
0	8	.171	0	.248	.0310	1.00
1-49	6	.155	0	.201	.0335	1.14
50-99	5	.153	1	.146	.0293	1.48
100-199	28	1.29	0	.899	.0321	2.21
200-399	15	1.27	2	.499	.0333	4.86
400+	13	2.96	3	.323	.0248	10.7
Total	75	5.99	6	2.32	—	—

1. Based on final model:

$$\text{Predicted} = \sum_S (1 + e^{-(.380 + \ln(\frac{r}{1-r}) + .00527X)})^{-1};$$

S: members of stratum; X: exposure to epoxy-like materials (exposure-months, weighted for latency and emphasizing pre-1960 exposures).

2. Expected number of colon cancer deaths in stratum, based on national age-, year-, sex-, race-, cause-specific proportional mortality rates, r; Expected = $n(\text{mean } r) = \sum r$
3. Predicted odds ratio: $OR = e^{(.00527X)}$; X chosen as stratum mid-point except for highest stratum where X = 450.

Table 21

**Logistic Regression Analysis of Association Between Death
Due to Ovarian Cancer and Exposures in Electronics Production (n=75)**

Model	Predictor ⁽¹⁾	Effect Estimate, SE	Removal from Model ⁽²⁾		Adj. OR ⁽³⁾	95% CI
			$\Delta(-2\ln L)$	P		
1.(4)	Intercept	-.344, 1.54	—	—	.71	
	(Cyanoacrylate) ^{0.5}	.127, .096	2.95	.04	7.15	.76, 67.5
	(Inspection) ^{0.5}	.320, .176	6.54	.005	11.9	1.78 79.6
2.	Intercept	.591, .822	—	—	1.81	
	Cyanoacrylate	.00384, .00288	1.88	.09	2.51	
	Inspection	.0208, .0112	4.66	.02	3.48	
3.	Intercept	1.270, .556	—	—	3.56	
	Cyanoacrylate	.00188, .00237	.52	.48	1.57	
4.	Intercept	1.214, .479	—	—	3.36	
	Inspection	.0156, .0098	3.31	.07	2.56	
5.	Intercept	1.727, 1.239	—	—	5.62	
	Epoxy	-.00317, .00802	.54	.23	.46	
	Inspection	.0121, .0135	—	—	2.07	
6.	Intercept	.579, .791	—	—	1.78	
	(EM/Micro-EM Ass'y) ^{0.5}	.174, .117	2.12	.07	3.85	
	(Inspection) ^{0.5}	.237, .125	5.21	.01	6.26	
7.	Intercept	1.047, .657	—	—	2.85	
	Motor/Winding	.00468, .0108	.23	.5	1.32	
	Inspection	.0170, .0105	—	—	2.77	
8.	Intercept	1.371, .513	—	—	3.94	
	Age at Death	-.0536, .0477	1.33	.13	.58	
	Inspection	.0180, .0129	—	—	2.94	

- Predictors are exposures (in exposure-months using latency-weighted durations and emphasizing pre-1960 exposures) or department durations (in months of latency-weighted duration, emphasizing the pre-1960 period) and age at death (years greater than age 55).
- Hypothesis testing consisted of removing a predictor from the model and assessing the change in $-2\ln(\text{likelihood})$, distributed as chi-squared; 1-tailed P-values were computed.
- The adj. OR for the intercept is the standardized mortality odds ratio estimated for the study population adjusting for the predictors in model, i.e., for the "unexposed." For exposure predictors, the adj. OR is the exposure odds ratio within the study population, standardized to the reference population and applied to 5 years (wt. duration) of exposure (and exposure level 4 where applicable). For age at death (model 8), the adj. OR is for a 10-yr. age increment. Confidence interval (95% CI) is based on chi-squared (test-based).

4. Final Model: $\ln\left(\frac{p}{1-p}\right) = -.344 + \ln\left(\frac{r}{1-r}\right) + .127X_1^{0.5} + .32X_2^{0.5}$

where: p = probability that death was due to ovarian cancer;
 r = age-, year-, race-, sex-specific proportional mortality rate for ovarian cancer in U.S.;
 X_1 = exposure to cyanoacrylate-like materials, in exposure-months;
 X_2 = duration in Inspection, in months.

Table 22

Logistic Regression Analysis of Association Between Death Due to Cancer of the Ovary and Exposure to Materials Including Cyanoacrylates and Related Adhesives, etc., and to Inspection: Goodness of Fit

Cyanoacrylate-like Exposure Strata (exposure-months)	n	Cases of Ovarian Cancer				
		Predicted ⁽¹⁾	Observed	Expected ⁽²⁾	r, mean ⁽²⁾	Pred. OR ⁽³⁾
0	24	2.173	3(4)	0.464	.0194	1.00
1-49	13	.852	1	0.352	.0271	1.89
50-99	7	.514	1	0.183	.0262	3.03
100-199	11	.957	0	0.301	.0273	4.79
200-399	13	1.447	2	0.293	.0225	9.16
400+	7	1.018	1	0.097	.0139	15.1
Total	75	6.96	7	1.69	—	—

1. Based on final model:

$$\text{Predicted} = \sum_S (1 + e^{-(.344 + \ln(\frac{r}{1-r}) + .1275X_1^{0.5} + .320X_2^{0.5})} - 1;$$

S: members of stratum; X_1 : exposure to cyanoacrylate-like materials, in exposure-months; X_2 : duration in Inspection, all durations weighted for latency and emphasizing the pre-1960 period.

2. Expected number of ovarian cancer deaths in stratum, based on national age-, year-, sex-, race-, and cause-specific proportional mortality rates, r ; expected = $n(\text{mean } r) = \sum r$.
3. Predicted odds ratio: $OR = e^{(.1275X_1^{0.5})}$; X_1 chosen as stratum mid-point except for highest stratum where $X_1 = 450$ was chosen.
4. Two ovarian cancer cases in the zero-level exposure stratum had long durations in Inspection.

Table 23
Logistic Regression Analysis of Association Between Death Due to
Cancer of Pancreas and Exposures in Electronics Production in Men (n=210)

Model	Predictor(1)	Effect Estimate, SE	Removal from Model(2)		Adj. OR(3)	95% CI
			$\Delta(-2\ln L)$	P		
1.(4)	Intercept	.166, .666	—	—	1.18	
	Epoxy, truncated(5)	.0278, .0110	5.55	.009	16.1	1.60, 163
	Inspection	.0191, .0115	2.40	.06	3.15	.73, 13.4
2.	Intercept	.300, .689	—	—	1.34	
	(Epoxy) ^{0.5}	.159, .0894	3.47	.03	11.7	
	Inspection	.0174, .0115	2.06	.08	2.83	
3.	Intercept	.630, .585	—	—	1.88	
	Epoxy	.00674, .00683	1.40	.12	5.03	
	Inspection	.0143, .0109	1.53	.11	2.36	
4.	Intercept	.590, .498	—	—	1.80	
	Epoxy, truncated(5)	.0231, .0097	4.35	.02	10.1	
5.	Intercept	.820, .446	—	—	2.27	
	Inspection	.0123, .0101	1.20	.5	2.09	
6.	Intercept	.733, .882	—	—	2.08	
	Solvent	.00600, .00485	.03	.5	4.22	
	Inspection	.0132, .0133	—	—	2.20	
7.	Intercept	1.047, .413	—	—	2.84	
	(Fabrication) ^{0.5}	-.0204, .1256	.02	.5	.98	
8.	Intercept	.917, .522	—	—	2.50	
	Age at Death	-.00951, .0271	.07	.5	.91	
	Inspection	.0123, .0101	—	—	2.09	

- Predictors are exposures (in exposure-months using latency-weighted durations and emphasizing pre-1960 exposures) or department durations (in months of latency-weighted duration, emphasizing the pre-1960 period) and age at death (years greater than age 55).
- Hypothesis testing consisted of removing a predictor from the model and assessing the change in $-2\ln(\text{likelihood})$, distributed as chi-squared; 1-tailed P-values were computed.
- The adj. OR for the intercept is the standardized mortality odds ratio estimated for the study population adjusting for the effect of the predictors in model, i.e., for the "unexposed." For exposure predictors, the adj. OR is the exposure odds ratio within the study population, standardized to the reference population and applied to 5 years (wt. duration) of exposure (and exposure level 4 where applicable). For age at death (model 8), the adj. OR is for a 10-yr. age increment. Confidence interval (95% CI) is based on chi-squared (test-based).

4. Final Model: $\ln\left(\frac{p}{1-p}\right) = .166 + \ln\left(\frac{r}{1-r}\right) + .0278X_1 + .0191X_2$

where: p = probability that death was due to cancer of the pancreas;
r = age-, year-, race-, sex-specific proportional mortality rate for cancer of pancreas in U.S.;
X₁ = exposure to epoxy-like materials in exposure-months and truncated: values greater than 100 set to equal 100;
X₂ = duration in Inspection, in months.

- Values greater than 100 set to equal 100; adj. OR based on 100 exposure-months.

Table 24

**Logistic Regression Analysis of Association Between Death Due to
Cancer of the Pancreas and Exposures to Epoxy-like Materials
and Inspection, in Men: Goodness of Fit**

Epoxy-like Exposure Strata (exposure-months)	n	Cases of Cancer of Pancreas				
		Predicted ⁽¹⁾	Observed	Expected ⁽²⁾	r, Mean ⁽²⁾	Pred. OR ⁽³⁾
0	133	3.12	2(4)	1.62	.0122	1.00
1-49	62	1.75	2(4)	.793	.0128	1.99
50-99	7	0.64	2	.077	.0110	7.98
100-199	4	0.68	1	.043	.0108	16.1
206-399	4	0.79	0	.052	.0129	16.1
Total	210	6.98	7	2.58		

1. Based on final model:

$$\text{Predicted} = \sum_S (1 + e^{-(.1659 + \ln(\frac{r}{1-r}) + .0278X_1 + .0191X_2)})^{-1};$$

S: members of stratum; X_1 : exposure to epoxy-like materials (exposure-months, truncated at 100); X_2 : duration in Inspection, all durations weighted for latency and emphasizing the pre-1960 period.

2. Expected number of pancreatic cancer deaths in stratum, based on national age-, year-, sex-, and race-specific proportional mortality rates, r ; expected = $n(\text{mean } r) = \sum r$.
3. Predicted odds ratio: $OR = e^{(.0278X_1)}$; X_1 chosen as stratum mid-point except for exposures above 100 where $X_1 = 100$.
4. Two pancreatic cancer cases, one in the zero-level of epoxy-like exposure and one in the 1-49 level, had long durations in Inspection.

Table 25

**Mantel-Haenszel Odds Ratios Comparing Kent County (Study Site)
and Genesee County for Selected Causes of Death¹**

Cause of Death	<u>Kent County</u>		<u>Genesee County</u>		MH-OR	X ²	95% CI
	Cases	Controls ²	Cases	Controls			
Colon Cancer In Women	469	12799	380	9963	1.013	.036	—
Pancreatic Cancer In Women	194	13074	136	10207	1.176	2.03	—
Ovarian Cancer In Women	304	12964	194	10149	1.371	11.4	1.14,1.64
Pancreatic Cancer In Men	235	16550	182	13494	1.076	.544	—

1. Based on all deaths 1970-82, of white men or women, stratified in 10 year age-at-death and 5 year year-of-death intervals.
2. Controls: all other causes of death from selected set consisting of ICD-8: 150-169, 180-208, 250-259, 410-419, 430-439, 490-599, 800-899.

APPENDIX

MODELING 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 by stratification on confounding covariates where feasible, as in case-control analysis (mortality odds ratios) or by estimation of covariate effects using logistic regression in case-control analysis.⁽²⁾

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 noncomparability 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. All of these limitations of SPMR studies apply to cohort or standardized mortality ratio studies (SMR) as well.

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

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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 is to model the odds of death having occurred due to some particular underlying cause compared with all other causes by using logistic regression:

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

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 five-year 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, and the coefficient b_1 is constrained to equal 1.0. The model is now:

$$\log \left(\frac{p}{1-p} \right) = a_0 + \log \left(\frac{r}{1-r} \right) + b_2X_2 + \dots$$

In the absence of any other effects (i.e., $b_2=b_3=\dots=0$) we would expect $a_0 = 0$ if the study population is a stratified random sample of the reference population. Otherwise, if selection is acting on the cohort, a_0 will reflect that selection, a_0 being an estimate of the (log) 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 model can be estimated using maximum likelihood procedures that allow specifying fixed values for some parameters (i.e., $b_1 = 1.0$), such as available in BMDP(3R).⁽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 modeled by the terms $b_i X_i$ 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. This is a proportional hazards formulation. 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): $b_{ij} X_i X_j$, where X_i is an exposure measure and X_j a chronological time measure, appropriately offset by some mean value. Including covariate main-effects in the model, such as age-at-death terms, would allow estimating a SMOR for the entire study population (adjusting for exposures) that was age-dependent — that is, the selection summarized by a_0 would depend on age at death.

Modeling 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.

One can describe exposure effects using the logistic regression-based model as follows: For the unexposed members of the study population,

$$\ln \left(\frac{p}{1-p} \right) \Big|_{x=0} = a_0 + \ln \left(\frac{r}{1-r} \right)$$

where a_0 is the parameter estimate, and p is the predicted probability that a death was due to a specified cause. For the exposed,

$$\ln \left(\frac{p}{1-p} \right) \Big|_{x \neq 0} = a_0 + \ln \left(\frac{r}{1-r} \right) + \sum b_i X_i$$

where b_i are the exposure effect estimates. These are both externally standardized predicted odds. The standardized exposure odds ratio is then given by:

$$OR(x) = \frac{\left(\frac{p}{1-p} \right) \Big|_{x_i \neq 0}}{\left(\frac{p}{1-p} \right) \Big|_{x_i = 0}} = \frac{e^{a_0 + \ln \frac{r}{1-r} + \sum b_i X_i}}{e^{a_0 + \ln \frac{r}{1-r}}} = e^{\sum b_i X_i}$$

This odds ratio is somewhat unconventional in that the standardization on covariates is based on an external population (e.g., U.S. national), while the exposure contrast is based on an internal comparison, within the study population.

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