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RESEARCH ARTICLE

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Mortality among autoworkers manufacturing electronics in Huntsville, Alabama

Nathan DeBono PhD | Kaitlin Kelly-Reif PhD | David Richardson PhD | Alex Keil PhD | Whitney Robinson PhD | Melissa Troester PhD | Stephen Marshall PhD

Department of Epidemiology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina

Correspondence
Nathan DeBono, PhD, Department of Epidemiology, University of North Carolina at Chapel Hill, Chapel Hill, NC, 27599.
Email: ndb@unc.edu

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Background: Workers raised concerns over suspected excesses of mortality at automotive electronics manufacturing facilities in Huntsville, Alabama.
Methods: A study of 4396 UAW members ever-employed at Huntsville facilities between 1972 and 1993 was conducted with mortality follow-up through 2016. Standardized Mortality Ratios (SMRs) were estimated using U.S. and Alabama reference rates.
Results: Relative to U.S. rates, there was a modest excess of all-cause mortality among White female workers (SMR 1.08, 95%CI: 0.99-1.18) and among all workers hired <1977 at the original plant building (SMR 1.10, 95%CI: 0.99-1.22). There was excess nervous system disorder (SMR 1.24, 95%CI: 0.91-1.65) and brain and nervous system cancer (SMR 1.31, 95%CI: 0.67-2.28) mortality. Estimates for several causes of interest were imprecise.
Conclusions: All-cause mortality estimates were greater than anticipated based on results from other UAW cohorts. The excess of nervous system disease mortality is consistent with other studies of electronics workers exposed to lead-solder and chlorinated solvents.

KEYWORDS
1,1,1-trichloroethane, electronics manufacturing, lead, mortality, occupational cohort, solder, trichloroethylene

1 | INTRODUCTION

Former employees at automotive electronics manufacturing facilities in Huntsville, Alabama have raised concerns over a suspected excess of mortality among their colleagues. The facilities were closed in 2010, however, public knowledge of soil contamination with chlorinated organic solvents at one plant site and asbestos contamination of at least one plant building has increased worker's concerns over potential health hazards associated with employment at the facilities. In 2015, local members of the United Autoworkers (UAW) produced an employee-generated list of deceased workers and requested that the UAW Health and Safety Department evaluate a perceived elevated rate of mortality among former employees. The UAW requested epidemiologic support to investigate worker concerns.

The Huntsville facilities primarily manufactured electronic printed circuit boards for automotive engine, body, and dashboard components for Chrysler and other manufacturers from 1971 to 2010. Interviews with former employees and UAW health and safety representatives at the facilities indicated that workers were exposed to trichloroethylene (TCE), lead fumes from molten solder, fiberglass dust, and asbestos in plant walls. Local news articles have reported that

Institution at which the work was performed: University of North Carolina at Chapel Hill.

soil and groundwater at one plant site are contaminated with chlorinated solvents and other industrial agents as confirmed by testing conducted in the 1990s.[1,2] Previous studies among workers employed at electronics and computer manufacturers in the U.S. have indicated exposure to lead-based solder and chlorinated solvents, including TCE and 1,1,1-trichloroethane, to be of particular concern for worker health due to the known toxicity of these agents to several major organ systems.[3–11] Previous mortality studies among hourly UAW members in the large UAW-Ford and UAW-GM cohorts reported lower standardized all-cause mortality rates among workers relative to the U.S. general population,[12,13] which is characteristic of "healthy worker" effects common in occupational studies of mortality.[14]

The objective of this study was to investigate concerns about excess mortality among 4396 hourly and salaried UAW members ever-employed at automotive electronics manufacturing facilities between 1972 and 1993 in Huntsville, Alabama. Cause-specific mortality rates in the study cohort were compared externally with U.S. and Alabama general population rates using standardized mortality ratio (SMR) analyses. Mortality estimates were stratified according to worker sex, race, and calendar period of first employment with examination of "healthy worker" effects. This investigation involved the enumeration of a novel cohort with primary ascertainment of mortality and cause of death.

2 | METHODS

2.1 | Study setting

Automotive electronics manufacturing operations began in Huntsville in 1971 at a plant building originally constructed for Chrysler defense and aerospace contracts in the 1950 (Plant 1). This original Plant 1 building was the site of all manufacturing until 1977, when a second plant (Plant 2) was built adjacent. Both Plant 1 and 2 were used as the primary site of manufacturing until 1989, when a large, more modern facility was constructed at a separate site (Plant 3). The majority of the workforce and equipment was transferred to Plant 3 after it opened, although Plant 1 and 2 remained in use for some manufacturing operations. A small manufacturing operation also existed at a fourth plant building to fulfill a military and railway electronics contract from 1983 to 1989. The workforce remained unionized through the UAW until all facilities in Huntsville were permanently closed in 2010.

2.2 | Study population

The study cohort includes 4396 hourly and salaried UAW members employed for any duration at any Chrysler electronics facility in Huntsville between 1972 and 1993. The cohort was enumerated for the purposes of this investigation from national UAW employment records generated through a joint UAW-Chrysler agreement. Individuals were selected into the study cohort from the national records if their work history contained a plant code corresponding to any of the Chrysler electronics facilities in Huntsville during the calendar years for which records were available (1967-1970 and 1972-1993). The employment records used for this investigation were updated biannually and include company work history for the entire study cohort during the observed employment period. The records were accessed in computerized format and included a skilled trade job code and yearly indications of employment at specific Chrysler plant codes. The three available plant codes at the Huntsville facilities correspond to Plant 1 and 2 (combined), the military plant, and Plant 3. The study cohort includes both hourly and salaried UAW members, as it was not possible to distinguish workers in each pay grade with the available data. The titles of skilled trade job codes could not be identified with available UAW information. Salaried UAW members generally worked in non-production, non-managerial jobs such as engineering or clerical work. It is estimated that approximately 10% of UAW members employed at the Huntsville facilities were salaried employees.

All individual employment records were linked with the most current version of the UAW pension information system at UAW offices (Solidarity House) in Detroit, Michigan to obtain missing birth date, sex, and race information and to verify information provided in the UAW employment records. A total of 3631 (83%) individuals in the cohort matched in the UAW pension system using the social security number (SSN). A subset of 952 records were additionally searched in a commercial public information database (LexisNexis Accurint) to obtain demographic information that remained missing after the pension linkage. The search included consumer/marketing and U.S. voter registration databases and was conducted using complete name and SSN. The search provided the birth date or sex for all individuals and race for 48% of the 883 individuals missing this information. A separate search of LexisNexis Accurint was also conducted to obtain the last known state of residence of all individuals in the study cohort to improve the search and match criteria of mortality follow-up. There were no exclusions applied to the study cohort based on missing data. The study protocol was approved by the (University of North Carolina at Chapel Hill) Institutional Review Board.

2.3 | Exposure characterization

An author (NDB) conducted interviews with eleven individuals formerly employed at the Huntsville facilities in-person as well as via phone and email in early 2017. Interviewees were contacted through representatives of the UAW Health & Safety Department and UAW Locals in Huntsville and included two former UAW health and safety representatives and at least one hourly and salaried employee, skilled tradesperson, chemical specialist (delivery), and chemical engineer employed at the facilities. Employment of interviewees spanned the entire operational history of all plants. Interviews were semi-structured and designed to provide information on plant history, manufacturing processes, and exposures of concern during the observed employment period. The author visited all plant sites in-person to corroborate information obtained in interviews.

Interviews identified lead, chlorinated solvents, fiberglass dust, conformal coatings, and asbestos as exposures of primary concern.

Workers reported inhalation and dermal exposure to lead through various soldering operations, including molten wave solder, hand solder, and solder paste processes. Chlorinated organic solvents, including TCE and 1,1,1-trichloroethane, were used at the facilities for resist and solder removal from circuit boards, machinery, tools, or worker's hands. UAW health and safety representatives were informed of soil contamination with chlorinated solvents at the Plant 2 site in the 1980s. Workers also reported particular concern over working conditions at the original Plant 1 building. Primary concerns at Plant 1 included a lack of ventilation in the production area, lack of enclosures or capture systems on wet processing lines, excessive heat, and asbestos in plant walls. A retrospective exposure assessment conducted at an IBM facility in New York state that also primarily manufactured electronic circuit boards corroborated worker testimony of the presence of TCE, 1,1,1-trichloroethane, lead-based solder, and fiberglass dust exposure in manufacturing processes.[4] The assessment also reported use of tetrachloroethylene and dichloromethane, although it is unknown whether these agents were used at the Huntsville facilities. At the IBM facility, workers were exposed to TCE <1985 only, and exposure was greatest for 1,1,1-trichloroethane throughout all manufacturing eras from 1969 to 2002. No quantitative exposure information or industrial hygiene monitoring data were available for this investigation. Job- and department-specific work history information was also unavailable for classifying work history according to specific exposure processes.

2.4 | Mortality and cause of death ascertainment

Vital status of the study cohort was ascertained through December 5th, 2016 using three sources: the Social Security Death Index (SSDI), the UAW pension information system, and the National Death Index (NDI). The entire cohort was searched for vital status ascertainment in the SSDI through December 5th 2016. The UAW pension system provided vital status through the UAW's internal administration of benefits from 1992 to 2016. A total of 653 individuals who were not identified as deceased and either: (i) did not match to the UAW pension system at all or (ii) had a missing or inactive residential address were also submitted for additional vital status follow-up in the NDI through December 2016. All sources provided each decedent's full date of death.

Individuals identified as deceased in any source had their cause of death ascertained using the underlying cause of death code listed on the death certificate. Death certificate information was obtained from the NDI for deaths occurring in 1979 or later (n = 1118). For deaths prior to 1979, death certificates were obtained from the Alabama state vital records office (n = 9). Both sources provided the underlying cause of death code classified according to the International Classification of Diseases (ICD) revision in effect at the time of death. There were seven individuals identified as deceased by the UAW pension system or SSDI with unknown cause of death. Of these, six did not match sufficiently in the NDI and one died prior to 1979 without a matching death certificate in Alabama state vital records. These seven individuals were identified as deceased for analyses (<1% of all decedents), as they were assumed to have died outside the U.S. or Alabama (prior to 1979), or had incomplete identifiable information listed on their death certificate. Individuals not identified as deceased in any source as of December 5th 2016 were presumed alive.

2.5 | Statistical analyses

SMR analyses comparing cause-specific mortality rates in the study cohort to that of the general population of the U.S. and Alabama were conducted using the National Institute of Occupational Safety and Health's Life Table Analysis System (NIOSH LTAS).[15] The SMRs for this investigation can be interpreted as a ratio of the observed to the expected number of deaths in the cohort, where the expected equals the number of deaths that would have been observed had the cohort experienced the same mortality rate as a given general population with the same age, sex, and race distribution during the same calendar years. This interpretation also assumes the person-time distribution in the study population would have remained unchanged had workplace exposures been absent.[16]

Person-time at risk began on the date of first employment at the Huntsville facilities and ended on December 5th 2016 for those presumed alive or the date of death for those deceased. For all SMRs, first employment dates were imputed at January 1st of the first year of observed work at the facilities. This date was chosen over a mid-year date so as not to exclude any individuals who died between January 1st and July 1st of the year they first worked, and adds a trivial amount of person-time to SMR calculations. Person-time at risk was stratified by age (5-year groups), calendar period (5-year intervals), binary race (White, Black or other), and sex and multiplied by the corresponding mortality rate in the referent populations to generate expected numbers of deaths. “Black or other” was defined as one racial category for analyses. Referent rates were based on national mortality rates in the U.S. general population from 1972 to 2012. Given that 80% of decedents died in Alabama, SMRs were also estimated using referent rates from the general population of Alabama from 1972 to 2014. Alabama rates were used for comparison to the SMRs estimated using national rates and to evaluate differences in trends of underlying cause of death coding in Alabama relative to the U.S. For all calendar years where referent mortality rates were unavailable (2013-2016 for the U.S. and 2015-2016 for Alabama), the rates for the most recent year with available data were repeated.

The SMR calculations are based on race-specific (White, Black or other) mortality rates given that mortality rates in the U.S. vary considerably between these groups. However, race was missing for 10% (n = 446) of the study cohort. Individuals with missing race were more likely to be born earlier (median year of birth 1943 vs 1949), first employed earlier (median year of hire 1977 vs 1983), and more likely to be deceased (59% vs 22%). SMRs were sensitive to the exclusion of individuals with missing race from analyses (complete case analysis)

given the high proportion of deaths in this group. In order to calculate SMRs for the entire cohort, we conducted a sensitivity analysis in which we imputed binary race (White, Black or other) for individuals missing this information. The imputation was conducted using a logistic regression model with covariates that were associated with race among individuals with non-missing race (sex, birth date, skilled trade status, plant ever/never worked, age of first employment). A single imputation was made for these analyses that assigned White race to 87% of individuals missing race, resulting in the analytic cohort being 81% White (compared to 80% White among those with known race). Estimates of the standard error of our SMRs were not adjusted because the proportion missing race was small (10%). Results of sensitivity analyses for the race imputation method are presented in supplementary Table SA, which compares analyses with: (i) the exclusion of individuals with missing race; (ii) re-imputed race with a lower proportion White (83%) among those missing race; and (iii) re-imputed race with a greater proportion White (91%) among those missing race.

SMRs using each referent population were stratified by sex and race to evaluate differences in mortality patterns according to these characteristics. Stratification was done using a cross-classification of the sex and race variables. Since building-specific work history was unavailable, SMRs were also stratified according to calendar period of first employment at the facilities to evaluate differences in mortality risk during specific eras of facility operation corresponding to the opening of new plant buildings (<1977 vs ≥1977, <1983 vs ≥1983, <1989 vs ≥1989). Analyses were also conducted to explore "healthy worker" effects in the study cohort, as SMR estimates in occupational cohorts typically show substantial deficits during periods of active employment and increase with increasing time since first hire.[17,18] SMRs were estimated using employed versus post-termination person-time and stratified according to time from company first hire to end of follow-up in 10-year intervals. Deaths occurring during employed person-time were those where the year of death was the same as the last calendar year of work.

For all SMRs, cause of death categories are based on the NIOSH-119 underlying cause of death classification scheme. Given the relatively small size of the cohort, statistical power was limited for several causes of death categories of interest. Estimates for all major and minor causes of death were examined with particular focus on causes of a priori interest identified based on known workplace exposures at the Huntsville facilities and other electronics plants in the U.S. with similar manufacturing processes. Causes of death of interest in this study include kidney cancer, lymphatic and hematopoietic malignancies including non-Hodgkin lymphoma, brain and nervous system cancer, liver cancer, non-malignant chronic kidney and liver diseases, and nervous system disorders for their association with TCE and 1,1,1-trichloroethane exposure. Additionally, cardiovascular diseases including hypertension and cerebrovascular disease, chronic kidney disease, and nervous system disorders were of interest for their association with occupational lead exposure. Respiratory system cancer and non-malignant lung disease were of interest due to their being caused by asbestos exposure.[19,20]

3 | RESULTS

Descriptive characteristics of the study cohort are presented in Table 1. The study cohort of 4396 workers was majority female (58%), White (80%), and had a median age of 66 years (Interquartile Range; IQR 59, 73) at the end of follow-up. There were 1134 individuals identified as deceased (26% of cohort) and the median age at death was 66 years (IQR 56, 75). The cohort accumulated a total of 143 427 person-years of follow-up with a median of 33 years per individual (IQR 29, 40). The majority (66%) of observed employed person-time occurred at Plant 1 and 2 between 1972 and 1988. There were 469 (11%) individuals in the cohort with ≤1 year of observed employment. The median observed time working at the facilities was 9 years (IQR 4, 12). There were 221 workers active during the first observed year of plant operation in 1972 and 2212 active during the last observed year in 1993.

3.1 | Mortality in the overall cohort

Table 2 presents estimates of relative cause-specific mortality in the overall cohort using both referent populations. After standardizing to the age, sex, race, and calendar year distribution of the study cohort, the all-cause mortality rate in the study cohort was similar to the U.S. general population referent rate (SMR 1.01, 95%CI 0.95-1.07). Relative to U.S. referent rates, there was a deficit of all-cancer mortality, however, mortality due to malignant neoplasms of the brain and nervous system (12 deaths, SMR 1.31, 95%CI 0.67-2.28), multiple myeloma (9 deaths, SMR 1.47, 95%CI 0.67–2.78), and esophageal cancer (10 deaths, SMR 1.22, 95%CI 0.59, 2.25) showed elevated but imprecise estimates of excess mortality. The number of observed deaths due to ischemic heart disease and hypertension with heart disease was lower than the expected number. However, there was a significant excess of mortality due to cardiac conduction disorders (66 deaths, SMR 3.74, 95%CI 2.89-4.76) and "other" heart diseases. There were no excesses of death due cerebrovascular disease or diseases of the arteries, veins, and lymphatic system. There was an indication of excess deaths due to hypertension without heart disease (11 deaths, SMR 1.32, 95%CI 0.66-2.36). For other causes of death of a priori interest, there was an excess of deaths due to nervous system disorders (46 deaths, SMR 1.24, 95% CI 0.91-1.65), which included an elevated but highly imprecise estimate for multiple sclerosis. There was also an excess in the number of deaths due to diseases of the genito-urinary system, including chronic and unspecified nephritis and renal failure (17 deaths, SMR 1.22, 95%CI 0.71-1.95).

SMR estimates using the Alabama referent rates were generally lower than those obtained using the U.S. rates and demonstrated equivalence or deficits between the observed and expected number of deaths for most causes (see Table 3). Using the

TABLE 1 Descriptive characteristics of 4396 hourly and salaried UAW members ever-employed at automotive electronics manufacturing facilities from 1972 to 1993 in Huntsville, Alabama

Characteristic	
N	4396
Year of birth, median (IQR)	1949 (1940, 1955)
Sex, *n* (%)	
Female	2562 (58)
Male	1834 (42)
Race, *n* (%)	
White	3170 (80)
Black/African-American	746 (19)
Hispanic	24 (1)
Other	10
Missing	446
Vital status at end of follow-up, *n* (%)	
Presumed alive	3262 (74)
Deceased	1134 (26)
Cause of death known	1127 (99)
Cause of death unknown	7 (1)
Person-years of follow-up, median (IQR)	33 (29, 40)
Person-years of follow-up, cumulative	143 427
Age at end of follow-up, median (IQR)	66 (59, 73)
Age at death, median (IQR)	66 (56, 75)
Person-years of employment, Huntsville, cumulative (%)	39 381 (100)
Huntsville electronics (1972-1988)	25 866 (66)
Military-Public electronics (1983-1989)	1169 (3)
New Huntsville electronics (1989-1993)	12 346 (31)
Calendar period of hire, *n* (%)	
1972-1978	1720 (39)
1979-1985	1995 (45)
1986-1993	681 (15)
Age at first hire, median (IQR)	32 (25, 41)
Year of first hire, median (IQR)	1983 (1977, 1984)
Years of employment, median (IQR)	9 (4, 12)
Ever-worked at other Chrysler plant, n(%)	914 (21)

IQR, interquartile range.

Alabama rates, there was a significant deficit in the all-cause SMR, and SMRs did not indicate excess mortality for several causes observed to be in excess using the U.S. rates, including cardiac conduction disorders, "other" heart diseases, hypertension without heart disease, nervous system disorders (overall), or diseases of the genito-urinary system. However, there was still a greater than expected number of deaths for malignant neoplasms of the brain and other nervous system sites (SMR 1.15, 95%CI 0.60-2.01), multiple myeloma (SMR 1.32, 95%CI 0.60-2.50), esophageal cancer (SMR 1.29, 95%CI 0.62-2.36), and multiple sclerosis (SMR 2.33, 95%CI 0.64-5.98).

3.2 | Mortality according to sex and race group

Table 3 presents sex-stratified SMR results among White workers using U.S. referent rates. Sex-stratified results for Black (or other) workers are shown in supplemental Table SB since there were only 168 deaths in this group and estimates were highly imprecise. Among White females, there was a small but relatively precise excess of all-cause mortality (SMR 1.08, 95%CI 0.99-1.18). SMRs were significantly elevated for cardiac conduction disorders and other heart diseases. For causes of a priori interest, there was an excess number of deaths due to nervous system disorders. There were also excesses observed for non-Hodgkin lymphoma and unspecified nephritis and renal failure, although estimates for these causes were imprecise. Among White males, the number of deaths due to all-causes was similar to the expected number. Cause-specific SMRs were significantly elevated for cardiac conduction disorders and "other" heart diseases. For causes of a priori interest, there was an excess number of deaths due to acute glomerulonephritis and renal failure, "other" (primarily liver) diseases of the digestive system, and nervous system disorders.

Among Black (or other) individuals, the number of deaths due to all causes was similar to the expected number among Black (or other) females, but showed a large deficit among Black (or other) males using U.S. referent rates (supplemental Table SB). Estimates for causes of a priori interest were highly imprecise. However, there were excesses of mortality due to all cancers (combined) and lymphatic and hematopoietic cancer among both Black (or other) females and males. There was some indication of excess mortality due to nervous system disorders and hypertension without heart disease among Black (or other) females and chronic nephritis and renal failure among Black (or other) males.

Results using Alabama referent rates showed the same pattern in sex- and race- stratified analyses to estimates obtained using U.S. referent rates (not shown). Using the Alabama referent, the all-cause SMR estimate was greatest among White females (SMR 0.92, 95%CI 0.84-1.01), followed by White males (SMR 0.82, 95%CI 0.75-0.90), Black (or other) females (SMR 0.75, 95%CI 0.61-0.91), and Black (or other) males (SMR 0.56, 95%CI 0.43-0.72). Cause-specific estimates tended to show greater deficits using Alabama versus U.S. referent rates given the elevated mortality rates in the state.

3.3 | Mortality according to employment characteristics

Table 4 presents SMR results among those hired before and after the construction of Plant 2 in 1977 using U.S. referent rates. Overall, SMR estimates were elevated in the early (<1977) compared to the late (≥1977) hire group. In the early hire group, there was a small excess in the number of deaths due to all-causes and a large but imprecise excess of deaths due to brain and other nervous system cancers. There

TABLE 2 Standardized mortality ratios comparing mortality due to select causes of death among 4396 UAW members ever-employed from 1972 to 1993 to U.S. and Alabama referent rates[a]

		U.S.			Alabama		
Cause of death	Obs	Exp	SMR	95%CI	Exp	SMR	95%CI
All Causes	1134	1128.0	1.01	0.95, 1.07	1365.9	0.83	0.78, 0.88
All Cancers	318	340.7	0.93	0.83, 1.04	373.1	0.85	0.76, 0.95
MN buccal & pharynx	4	5.5	0.72	0.20, 1.85	5.8	0.69	0.19, 1.77
MN digestive & peritoneum	63	78.0	0.81	0.62, 1.03	77.3	0.82	0.63, 1.04
MN esophagus	10	8.2	1.22	0.59, 2.25	7.8	1.29	0.62, 2.36
MN liver, biliary passages, gall bladder	9	11.9	0.76	0.35, 1.43	11.9	0.75	0.34, 1.43
MN respiratory	100	104.6	0.96	0.78, 1.16	126.1	0.79	0.65, 0.96
MN of trachea, bronchus, lung	96	101.3	0.95	0.77, 1.16	122.7	0.78	0.63, 0.96
MN breast	36	33.2	1.09	0.76, 1.50	33.1	1.09	0.76, 1.51
MN female genital organs	18	20.2	0.89	0.53, 1.41	19.9	0.91	0.54, 1.43
MN male genital organs	11	10.6	1.03	0.52, 1.85	11.4	0.97	0.48, 1.73
MN urinary	8	13.9	0.58	0.25, 1.14	12.9	0.62	0.27, 1.22
MN kidney	1	7.7	0.13	0, 0.72	7.4	0.14	0, 0.75
MN bladder & other urinary site	7	6.1	1.14	0.46, 2.35	5.5	1.27	0.51, 2.63
MN other & unspecified site	47	44.3	1.06	0.78, 1.41	54.8	0.86	0.63, 1.14
MN brain & other nervous system	12	9.2	1.31	0.67, 2.28	10.4	1.15	0.60, 2.01
MN lymphatic & hematopoietic	31	30.5	1.02	0.69, 1.44	31.9	0.97	0.66, 1.38
Non-Hodgkin's lymphoma	12	11.9	1.01	0.52, 1.76	12.1	0.99	0.51, 1.73
Multiple myeloma	9	6.1	1.47	0.67, 2.78	6.8	1.32	0.60, 2.50
Leukemia	10	11.4	0.88	0.42, 1.61	12.1	0.83	0.40, 1.52
Benign & unspecified neoplasms	3	4.1	0.72	0.15, 2.12	4.6	0.65	0.13, 1.91
Heart diseases	259	264.4	0.98	0.86, 1.11	338.2	0.77	0.68, 0.86
Hypertension with heart disease	5	14.6	0.34	0.11, 0.80	11.1	0.45	0.15, 1.05
Ischemic heart disease	130	190.4	0.68	0.57, 0.81	189.8	0.68	0.57, 0.81
Conduction disorder	66	17.6	3.74	2.89, 4.76	67.4	0.98	0.76, 1.25
Other heart diseases	44	20.5	2.15	1.56, 2.89	50.6	0.87	0.63, 1.17
Other diseases of the circulatory system	94	83.3	1.13	0.91, 1.38	107.3	0.88	0.71, 1.07
Cerebrovascular disease	60	52.4	1.14	0.87, 1.47	68.5	0.88	0.67, 1.13
Hypertension without heart disease	11	8.4	1.32	0.66, 2.36	10.7	1.03	0.51, 1.85
Diseases of the arteries, veins, lymph	23	22.5	1.02	0.65, 1.54	28.1	0.82	0.52, 1.23
Diseases of the genito-urinary system	25	22.4	1.12	0.72, 1.65	31.1	0.80	0.52, 1.19
Acute glomerulonephritis & renal failure	5	2.7	1.86	0.60, 4.33	4.2	1.19	0.39, 2.78
Chronic nephritis & renal failure	17	14.0	1.22	0.71, 1.95	19.7	0.86	0.50, 1.38
Diseases of the digestive system	55	50.2	1.10	0.83, 1.43	56.2	0.98	0.74, 1.27
Cirrhosis & other liver diseases	24	24.0	1.00	0.64, 1.49	23.9	1.00	0.64, 1.49
Other diseases of the digestive system	26	21.5	1.21	0.79, 1.77	27.0	0.96	0.63, 1.41
Diseases of the respiratory system	98	94.3	1.04	0.84, 1.27	120.7	0.81	0.66, 0.99
Chronic obstructive pulmonary disorder	55	56.1	0.98	0.74, 1.28	75.9	0.72	0.55, 0.94
Asbestosis	1	0.2	5.61	0.14, 31.3	0.4	2.65	0.07, 14.8
Nervous system disorders	46	37.2	1.24	0.91, 1.65	45.4	1.01	0.74, 1.35
Multiple sclerosis	4	2.7	1.50	0.41, 3.85	1.7	2.33	0.64, 5.98
Other nervous system diseases	42	34.5	1.22	0.88, 1.64	43.7	0.96	0.69, 1.30

(Continues)

TABLE 2 (Continued)

		U.S.			Alabama		
Cause of death	Obs	Exp	SMR	95%CI	Exp	SMR	95%CI
Mental & psychiatric disorders	23	26.7	0.86	0.55, 1.29	32.9	0.70	0.44, 1.05
Diabetes mellitus	28	35.9	0.78	0.52, 1.13	38.6	0.73	0.48, 1.05
Musculoskeletal & connective tissue diseases	4	6.0	0.67	0.18, 1.71	6.5	0.61	0.17, 1.57
Diseases of skin & subcutaneous tissue	1	1.6	0.63	0.02, 3.50	1.8	0.57	0.01, 3.15
Diseases of blood & blood forming organs	1	5.5	0.18	0, 1.01	6.9	0.14	0, 0.81
Tuberculosis & HIV	2	13.5	0.15	0.02, 0.54	7.1	0.28	0.03, 1.01
Transportation injuries	44	24.0	1.83	1.33, 2.46	36.3	1.21	0.88, 1.63
Falls	7	8.0	0.88	0.35, 1.81	5.3	1.31	0.53, 2.70
Other injury	24	25.0	0.96	0.62, 1.43	31.8	0.75	0.48, 1.12
Violence	38	30.2	1.26	0.89, 1.73	36.2	1.05	0.74, 1.44
Intentional self-harm	24	20.0	1.20	0.77, 1.78	22.1	1.09	0.70, 1.61
Symptoms & ill-defined conditions	24	13.6	1.76	1.13, 2.62	37.6	0.64	0.41, 0.95
Other & unspecified causes	40	41.6	0.96	0.69, 1.31	48.3	0.83	0.59, 1.13

Obs, observed number of deaths in study cohort; Exp, expected number of deaths in study cohort based on general population rates; MN, malignant neoplasm; SMR, standardized mortality ratio; CI, confidence Interval.

[a]Referent rates are standardized according to the age, sex, race, and calendar year distribution of the study cohort.

was an excess number of deaths for several causes of a priori interest, including cerebrovascular disease, diseases of the genito-urinary system, and digestive system diseases. In the late hire group, SMR estimates showed deficits or equivalences in mortality for most causes of death with the exception of a moderate excess observed for nervous system disorders. In both groups, the all-cause SMR increased monotonically with increasing time from first hire to end of follow-up. SMRs generally remained elevated in the early hire group relative to the late hire group in all categories of years since first hire, including the ≥30 year category. There was little evidence of differences in relative mortality using other (1983 and 1989) calendar year stratifications (not shown).

Table 5 presents SMR results according to observed employed and post-termination person-time using U.S. referent rates. During employment, there were large deficits in mortality due to all-causes and for all major cause of death categories. After termination of employment, there was a small but significant excess of all-cause mortality in the study cohort. There were also small but precise estimates indicating excesses of mortality due to cerebrovascular disease, diseases of the digestive system, and nervous system disorders. SMR estimates for nearly all causes of death were greater during the period after termination of employment than during the total at-risk period from first employment to end of follow-up.

4 | DISCUSSION

The overall study cohort exhibited an all-cause mortality rate similar to that of the U.S. general population standardized to the age, sex, race, and calendar-year characteristics of the study cohort. However, the relative all-cause mortality rate in the study cohort is greater than that reported in other UAW-based cohorts, as the company-wide UAW-Ford cohort of nearly 200 000 hourly employees and the UAW-GM cohort of over 45 000 hourly metalworkers in Michigan, both reported small deficits in all-cause mortality relative to the U.S. population with similar lengths of follow-up.[12,13] The greater all-cause SMR estimate in the study cohort relative to the UAW-Ford cohort persisted with stratification according to all sex- and race-specific subgroups except for non-White males, who had similar estimates. Our results also showed that workers hired prior to 1977 at the original Plant 1 building had a greater standardized all-cause mortality rate relative to U.S. referent rates, which is consistent with worker concerns over adverse working conditions and elevated exposure at this facility. Typically, estimates of lower-than-expected all-cause mortality relative to general population rates are reported in occupational studies due to "healthy worker" hire effects, whereby relatively healthier individuals are more likely to seek and be offered employment.[14] In this study, however, we did not observe a deficit in all-cause mortality in the overall cohort relative to U.S. referent rates, and we observed small excesses of all-cause mortality among women and pre-1977 hires. For mortality due to specific causes of a priori interest based on lead, TCE, and 1,1,1-trichloroethane exposure, we observed moderate excesses of brain and nervous system cancer mortality and non-malignant nervous system disorder mortality in the study cohort.

Previous studies of mortality hazards associated with electronics manufacturing occupations in the U.S. consist primarily of analyses of employees at IBM facilities.[3,5,21,22] Researchers at NIOSH conducted a mortality investigation among 34 494 workers employed at an IBM facility in New York state that also primarily manufactured electronic circuit boards in response to complaints over chlorinated solvent contamination of surrounding soil and groundwater.[3] At the IBM facility, historical exposure reconstruction estimated that large

TABLE 3 Standardized mortality ratios comparing mortality due to select causes of death among White female and White male UAW members ever-employed from 1972 to 1993 to U.S. referent rates[a] (estimates for Black or other females and males shown in supplemental Table SB)

	White females			White males		
Cause of death	Obs	SMR	95%CI	Obs	SMR	95%CI
All causes	475	1.08	0.99, 1.18	491	0.99	0.90, 1.08
All cancers	135	0.92	0.77, 1.09	122	0.86	0.72, 1.03
MN urinary	2	0.48	0.06, 1.74	6	0.73	0.27, 1.59
MN other & unspecified site	16	0.90	0.52, 1.47	25	1.18	0.76, 1.74
MN brain & other nervous system	7	1.76	0.71, 3.63	4	0.90	0.24, 2.30
MN lymphatic & hemaopoietic	9	0.75	0.34, 1.42	14	0.97	0.53, 1.64
Non-Hodgkin's lymphoma	6	1.23	0.45, 2.68	5	0.86	0.28, 2.02
Heart diseases	101	1.16	0.94, 1.41	132	0.99	0.83, 1.17
Ischemic heart disease	45	0.76	0.55, 1.01	73	0.70	0.55, 0.89
Conduction disorder	23	3.35	2.12, 5.02	36	4.81	3.37, 6.65
Other heart diseases	22	2.56	1.60, 3.87	16	1.89	1.08, 3.07
Other circulatory system diseases	41	1.17	0.84, 1.59	37	1.21	0.85, 1.66
Cerebrovascular disease	29	1.28	0.85, 1.83	20	1.08	0.66, 1.66
Diseases of the genito-urinary system	10	1.12	0.54, 2.06	9	1.13	0.52, 2.14
Acute glomerulonephritis & renal failure	1	0.89	0.02, 4.93	4	3.72	1.01, 9.51
Chronic nephritis & renal failure	8	1.59	0.69, 3.13	4	0.79	0.22, 2.02
Diseases of the digestive system	21	1.13	0.70, 1.73	27	1.17	0.77, 1.71
Cirrhosis & other liver diseases	9	1.23	0.56, 2.33	11	0.88	0.44, 1.58
Other diseases of the digestive system	10	1.10	0.53, 2.02	15	1.73	0.97, 2.86
Nervous system disorders	25	1.33	0.86, 1.96	18	1.25	0.74, 1.98
Multiple sclerosis	3	1.90	0.39, 5.55	1	1.39	0.04, 7.73
Other nervous system diseases	22	1.28	0.80, 1.93	17	1.25	0.73, 1.99
Transportation injuries	16	2.42	1.38, 3.93	21	1.57	0.97, 2.41

Obs, observed number of deaths in the study cohort; MN, malignant neoplasm; SMR, standardized mortality ratio; CI, confidence interval.
[a]Referent rates are standardized according to the age, sex, race, and calendar year distribution of the study cohort.

proportions of the cohort were ever-exposed to chlorinated solvents (mainly TCE and 1,1,1-trichloroethane) and lead-based solder.[4] External comparison results from the NIOSH investigation indicated large deficits of mortality due to all causes and all cancers among hourly males and females relative to U.S. referent rates, however, there was a significant excess of deaths due to non-Hodgkin lymphoma (SMR 1.49, 95%CI 1.15-1.89) among hourly males. Internal comparison results indicated that ≥5 years of employment in a circuit board manufacturing building was significantly associated with an elevated rate of leukemia mortality and that cumulative tetrachloroethylene exposure was significantly associated with elevated rate of nervous system disease mortality. Our results showed no evidence of excess mortality due to non-Hodgkin lymphoma, leukemia, or lymphatic and hematopoietic (overall) cancer mortality, however, we observed a moderate excess of nervous system disorder mortality. Investigators of the IBM cohort suggested that the youth of the cohort and low proportion of decedents limited the inferences able to be made from their results, as the mean age of hourly workers surviving to the end of follow-up was only 59 years.

Our findings indicated a moderate excess of non-malignant nervous system disorder mortality in the study cohort compared to U.S. referent rates. Nervous system disorders were of particular a priori interest in this investigation given that both lead and chlorinated solvents are toxic to the central nervous system.[6,7,10,23,24] A review by the U.S. Environmental Protection Agency (EPA) concluded the central nervous system to be the most sensitive target for 1,1,1-trichloroethane toxicity in humans.[7] Our estimate of excess nervous system disorder mortality in the overall cohort was precise and close to statistical significance, with an excess of similar magnitude observed in both male and female workers. The excess was concentrated almost exclusively among those hired in 1977 or later, with 25% of nervous system disorder decedents hired in exactly 1977, when 729 individuals were hired at the facilities presumably to help staff the newly constructed Plant 2. The excess among those hired in 1977 or later could be attributed to greater mean 1,1,1-trichloroethane exposure through increased use of this chemical in processes after the construction of the Plant 2 building. This building was also the site of soil contamination with 1,1,1-trichloroethane and other chlorinated

TABLE 4 Standardized mortality ratios comparing mortality due to select causes of death among 4396 UAW members to U.S. referent rates[a] according to hire period and years since first hire

	Years since first hire to end of follow-up										
	<10		10 to <20		20 to <30		≥30		Overall		
Cause of death	Obs	SMR	Obs	SMR	Obs	SMR	Obs	SMR	Obs	SMR	95%CI
First hired <1977 (*n* = 905)											
All causes	26	0.85	57	1.05	97	1.07	199	1.18	379	1.10	0.99, 1.22
All cancers	9	1.13	14	0.79	28	0.95	51	1.10	102	1.00	0.82, 1.22
MN other & unspecified site	1	0.89	3	1.32	6	1.65	13	2.26	23	1.80	1.14, 2.70
MN brain & other nervous	1	3.41	-	-	2	2.80	3	3.04	6	2.40	0.88, 5.23
Non-Hodgkin's lymphoma	-	-	-	-	2	1.80	2	1.20	4	1.10	0.30, 2.81
Heart diseases	3	0.37	21	1.39	30	1.25	40	0.99	94	1.07	0.87, 1.31
Cerebrovascular disease	-	-	-	-	7	1.49	17	1.85	24	1.37	0.88, 2.04
Diseases of the genitourinary system	-	-	2	3.19	3	1.82	6	1.33	11	1.55	0.77, 2.78
Diseases of the digestive system	1	0.52	4	1.53	5	1.34	9	1.48	19	1.32	0.80, 2.07
Nervous system disorders	-	-	1	1.33	1	0.45	11	1.25	13	1.07	0.57, 1.83
First hired ≥1977 (*n* = 3491)											
All causes	63	0.63	167	0.91	314	1.04	211	1.07	755	0.96	0.90, 1.04
All cancers	17	0.64	55	0.93	91	0.95	53	0.91	216	0.90	0.79, 1.03
MN other & unspecified site	2	0.49	8	1.01	8	0.65	6	0.83	24	0.76	0.49, 1.13
MN brain & other nervous	-	-	3	1.66	1	0.40	2	1.47	6	0.90	0.33, 1.96
Non-Hodgkin's lymphoma	-	-	4	1.85	4	1.27	-	-	8	0.97	0.42, 1.90
Heart diseases	15	0.71	35	0.81	69	1.01	46	1.04	165	0.93	0.80, 1.09
Cerebrovascular disease	2	0.57	6	0.79	16	1.16	12	1.21	36	1.03	0.72, 1.43
Diseases of the genitourinary system	1	1.04	1	0.37	5	0.76	7	1.38	14	0.91	0.50, 1.53
Diseases of the digestive system	-	-	7	0.78	20	1.46	9	1.14	36	1.00	0.70, 1.39
Nervous system disorders	-	-	3	0.84	10	0.95	20	2.10	33	1.32	0.91, 1.85

Obs, observed number of deaths in the study cohort; MN, malignant neoplasm; SMR, standardized mortality ratio; CI, confidence interval.
[a]Referent rates are standardized according to the age, sex, race, and calendar year distribution of the study cohort.

solvents in the mid-1980s, suggesting workers there may have been more highly exposed to these chemicals through vapor intrusion into the facility, contaminated plant drinking water affected by groundwater infiltration, or the disposal of solvents into containment systems. The soil contamination also occurred on a recreational area and baseball field adjacent to the plant building used by workers during break times. The observed excess of mortality due to nervous system disorders in the overall cohort was driven by both multiple sclerosis mortality, which showed a large but highly imprecise excess relative to both U.S. and Alabama referent rates, as well as "other" nervous system diseases, which consisted of a majority of deaths due to Alzheimer's and Parkinson's disease. Cause of death reporting on death certificates is relatively insensitive to the ascertainment of nervous system disorders, as neurological conditions are less likely to be reported compared to other competing causes of death.[25,26] However, we do not expect the ascertainment of nervous system disorder mortality in the cohort to be more sensitive than that reflected in national rates. Our finding of excess nervous system disorder mortality in the study cohort is consistent with results from the company-wide analysis of decedents employed at IBM, where the proportion of nervous system disorder deaths was reported to be in statistically significant excess compared to the U.S. referent (point estimate not provided).[5]

Our results indicated a moderate excess in mortality in the study cohort due to malignant neoplasms of the brain and other parts of the nervous system. Estimates for this cause should be treated with caution since they are based on only 12 deaths due to the rare incidence of these cancers, however, the excess was observed using both referent populations. The excess was substantially more pronounced among those hired before 1977, when overall exposure to plant processes was presumed to be greatest and operations were confined to the original Plant 1 building with more limited worker protections. Several previous studies have shown employment in electronics manufacturing jobs to be associated with elevated risk of brain or nervous system cancer mortality.[5,22,27–30] A company-wide analysis of 31 941 decedents employed for at least 5 years at IBM in the U.S. found a significantly elevated proportion of brain and nervous system cancer deaths among hourly male manufacturing

TABLE 5 Standardized mortality ratios comparing mortality due to select causes of death among 4396 UAW members to U.S. referent rates[a] according to employment status

	Employed			Post-termination		
Cause of death	Obs	SMR	95%CI	Obs	SMR	95%CI
All causes	67	0.51	0.39, 0.64	1,067	1.07	1.01, 1.14
All cancers	16	0.43	0.25, 0.70	302	0.99	0.89, 1.11
MN other & unspecified site	2	0.37	0.05, 1.35	45	1.16	0.84, 1.55
MN brain & other nervous	1	0.74	0.02, 4.14	11	1.40	0.70, 2.51
Heart diseases	20	0.68	0.42, 1.05	239	1.02	0.89, 1.15
Conduction disorder	4	1.93	0.53, 4.94	62	3.98	3.05, 5.10
Cerebrovascular disease	-	-	-	60	1.27	0.97, 1.63
Diseases of the genitourinary system	-	-	-	25	1.19	0.77, 1.75
Diseases of the digestive system	1	0.13	0, 0.75	54	1.26	0.95, 1.65
Nervous system disorders	-	-	-	46	1.30	0.95, 1.74

Obs, observed number of deaths in study cohort; SMR, standardized mortality ratio; CI, confidence interval.
[a]Referent rates are standardized according to the age, sex, race, and calendar year distribution of the study cohort.

workers relative to the U.S. population.[5] This finding is consistent with results from an analysis of 583 deceased hourly UAW members employed at an aerospace electro-mechanical systems facility, which also reported an elevated proportion of brain and nervous system cancer mortality.[30] A case-control study of 2173 male brain cancer decedents identified through occupational mortality surveillance in the U.S. between 1985 and 1986 also reported a significantly elevated odds of mortality associated with electrical work in manufacturing industries.[29] Exposure to specific chlorinated solvents used in electronics manufacturing has also been associated with brain or nervous system cancer in other studies,[31–33] including one study that included biological measurements of exposure to three chlorinated solvents and cancer incidence follow-up in Finland,[34] although evidence for this relationship remains inconsistent.[35,36]

Our results showed that workers hired prior to 1977 experienced an elevated all-cause mortality rate relative to the U.S. general population and also a greater mortality ratio than those hired during or after 1977. The finding of elevated mortality in the pre-1977 hire group is consistent with UAW members' concerns over hazards at the original Plant 1 building, which was used exclusively from 1972 to 1977. Working conditions at Plant 1 were described as being the most adverse, with no ventilation system in the production area and limited protections from lead-solder or chlorinated solvent exposure. At the IBM facility in New York state, mean cumulative exposure in the workforce to TCE and 1,1,1-trichloroethane was greatest in earlier calendar eras of operation.[4] In the pre-1977 hire group, estimates indicated excess mortality for all major causes of a pirori interest with the exception of nervous system disorders. The greater all-cause mortality ratio among pre- versus post-1977 hires persisted after stratification of person-time by number of years from first hire to end of follow-up. While this stratification may not have fully accounted for differences in mean length of follow-up between groups, the observation of elevated mortality in the pre-1977 hire group is consistent with UAW members' descriptions of exposure history at the facilities, and stratification by the median year of hire (1983) did not show any meaningful differences in all-cause or cause-specific relative mortality rates between hire groups. Despite the construction of Plant 2 in 1977 and the more modern Plant 3 in 1989, Plant 1 was used up until the final closure of all facilities in 2010, suggesting a significant portion of the cohort worked in the Plant 1 building throughout the study period.

Other causes of death of note in the cohort include one death due to asbestosis and one death due to toxic effects of non-petroleum solvent exposure, which is a category that includes chlorinated hydrocarbon solvents. Asbestos was reported by UAW members to be present in at least one of the original plant buildings. There were also three deaths due to spinal muscular atrophy and related syndromes, which includes amyotropic lateral sclerosis (ALS). ALS is a nervous system disorder that has been shown to be associated with chronic occupational lead exposure in a meta analysis,[37] although external comparisons for this cause of death could not be performed due to lack of more specific cause of death data and corresponding referent rates. We did not observe excesses of mortality for causes strongly related to smoking. The rate of death due to trachea, bronchus, and lung cancer and chronic obstructive pulmonary disease (COPD) in the study cohort was the same as the U.S. referent rate, suggesting that patterns and prevalence of smoking in the study cohort were similar to the U.S. average.

Our results showed evidence of "healthy worker" effects as anticipated. We observed a lower mortality ratio estimate among Black (or other) female and male workers compared to their White female and male counterparts, respectively. This finding is consistent with external comparison results from the UAW-Ford cohort and is potentially due to the larger disparity in mortality between Black (or other) workers and the U.S. general Black (or other) population, who suffer from a greater all-cause mortality rate than the general White population. We also observed a significant excess of all-cause

mortality in the cohort after observed termination of employment, which has been shown previously in other occupational cohorts.[18] This estimate is likely conservative given that the actual date of termination was in fact later than the last year of available work history for approximately half the cohort (n = 2,212). Our analysis of excess mortality stratified according to number of years from first hire to end of follow-up showed a monotonic increase in all-cause mortality estimates with increasing time since hire. This is consistent with the phenomenon of worker health status regressing to the general population average over time typically observed in occupational cohort studies, which can lead to underestimations of mortality risk associated with exposures at work.[17]

Results obtained using Alabama referent rates were subject to a stronger "healthy worker" effect than those using U.S. referent rates. We observed large deficits in all-cause and cause-specific mortality relative to Alabama referent rates, which was anticipated given that Alabama has had one of the highest age-adjusted all-cause mortality rates and one of the lowest median house hold incomes in the U.S. since at least the early 2000s.[38,39] These characteristics make the Alabama general population a problematic comparison group, as individuals in the study cohort who are able to maintain employment in a unionized occupation with above average health insurance, wages, and retirement benefits may be at a considerable mortality advantage relative to the Alabama average. Further, at least 21% of the study cohort worked at other non-Huntsville Chrysler plants, suggesting a sizeable proportion of the cohort may possess health-related lifestyle behaviors more characteristic of populations from other regions of the U.S. For these reasons, Alabama was considered a less suitable comparison population for the study cohort and results obtained using U.S. referent rates were used as the focus for analyses and discussion. Estimates obtained using Alabama referent rates were more useful for evaluating state-specific cause of death coding practices, as a large majority (80%) of decedents died in Alabama.

Cardiovascular diseases were of a priori interest in this study given that lead causes hypertension even at low levels of exposure and has been associated with stroke, ischemic heart disease, and peripheral arterial disease.[11] Cardiac arrhythmias and other more acute cardiac effects have also been associated with occupational exposure to chlorinated solvents, including 1,1,1-trichloroethane and TCE.[40] However, the interpretation of results for cardiovascular diseases in this study is hampered by the elevated baseline incidence of hypertension and cardiovascular disease mortality in the southeast U.S. and atypical coding practices for certain cardiovascular causes of death in this region.[41] We found a statistically significant threefold increase in cardiac conduction disorder mortality (a broad category of disorders including cardiac arrest) in the study cohort relative to U.S. referent rates, but this excess disappeared entirely when compared to referent rates in Alabama. The age-adjusted rate of cardiac conduction disorder mortality in Alabama from 1999 to 2016 is the highest in the U.S. and well exceeds that of the next highest states.[38] The observed excess of cardiac conduction disorders is likely a result of cause of death coding practices in Alabama, as the proportion of cardiac conduction disorder deaths among decedents who died in Alabama was significantly greater than that among decedents who died in other states (7% vs 0.8%, respectively). We also observed a significant excess of mortality for "other" heart diseases relative to the U.S. referent rates that showed a deficit relative to Alabama rates, which may also be attributed to Alabama-specific coding practices. In addition, hypertension has been shown to be underreported as an underlying cause of death on death certificates across the U.S.[42] Characterization of cardiovascular disease risks, including hypertension and stroke, may be better conducted through internal comparisons to improve the interpretability of results.

Our results showed little evidence of excess mortality for the a priori causes of interest of lymphatic and hematopoietic cancer, kidney diseases, and liver diseases. Estimates for several minor causes in these disease categories were too imprecise to make inferences. The International Agency for Research on Cancer (IARC) monograph on chlorinated solvents concluded that TCE exposure causes kidney cancer and has been associated with non-Hodgkin lymphoma and liver cancer in several studies.[43,44] We observed only one kidney cancer death and estimates indicated a significant deficit of deaths due to this cause in all analyses. There was also no excess of deaths due to non-Hodgkin lymphoma. These findings could be explained by either a low prevalence of TCE exposure or an inadequate length of follow-up, as the median age at death in the U.S. for both kidney cancer and non-Hodgkin lymphoma is 5 and 10 years greater than the median age of the cohort (66 years), respectively.[45,46] Our results did suggest a moderate excess of deaths due to multiple myeloma using both referent populations, although estimates were based on only nine deaths and were highly imprecise. Several well-designed studies have shown chlorinated solvent exposure to be associated with risk of multiple myeloma, with the strongest relationship purported for 1,1,1-trichloroethane exposure.[34,47–50] Diseases of the kidney and liver were of a priori interest as lead and TCE are toxic to the kidney, and TCE and 1,1,1-trichloroethane have demonstrated liver toxicity.[6,7,9,51] Estimates were suggestive of excess mortality for acute glomerulonephritis and renal failure relative to both the U.S. and Alabama referent rates, but were highly imprecise. There was little indication of excess mortality due to malignant or non-malignant liver diseases in the cohort.

For causes of death not of a priori interest, we observed elevated mortality rates due to esophageal cancer and transportation injuries. Estimates for esophageal cancer suggested an excess of death due to this cause relative to both the U.S. and Alabama referent rates, although the estimate was based on only 10 deaths and was imprecise. Previous studies indicate a limited and inconsistent relationship between chlorinated solvent exposure and esophageal cancer, although studies among dry cleaning workers have reported more consistent associations specific to tetrachloroethylene exposure.[40,47] Overall there is little evidence that exposure to fiberglass dust or asbestos is associated with esophageal cancer.[19,52] There was a large and significant excess of mortality due to transportation injuries in the cohort relative to U.S. referent rates. The estimate was attenuated but still

suggestive of an excess relative to Alabama referent rates. The excess of transportation injury mortality could be attributed to a variety of factors, including alcohol use, local roadway and traffic characteristics, or commute patterns among individuals in the cohort. It is also possible that the excess could be related to balance and coordination impairment caused by neurotoxic effects of lead and chlorinated solvents in the workplace. Transportation injury mortality was previously observed to be in significant excess among workers at a lead smelter in Idaho relative to U.S. referent rates.[53]

The primary limitation of this study is the lack of exposure assessment. We were unable to identify job- or department-specific work history or distinguish between hourly and salaried employees with available data. In general, there was good concordance between sources used to ascertain the presence of specific exposures at the facilities, but the prevalence and intensity of exposures in the cohort over time remains unknown. This limited the interpretation of our results for specific causes of interest and reduced our ability to compare findings with other studies in similar cohorts. Given that salaried workers likely had lower average exposure compared to their hourly counterparts by working less in production areas and having reduced process-specific exposures, the inability to identify salaried workers in analyses may have biased our estimates toward the null value, making our assessment of mortality risks in the cohort more conservative. A second limitation of this study is the lack of ascertainment of disease incidence. The use of mortality outcomes underestimated the actual burden of disease in the cohort for several diseases of interest, particularly those that are less often fatal or less likely to be reported as the underlying cause of death on death certificates. Additionally, the misclassification of cause of death coding, particularly for deaths potentially misclassified as being due to cardiovascular diseases in Alabama, may have biased our mortality ratio estimates for other causes downward. Due to the relatively small size of the cohort, estimates for several causes of interest were imprecise and limited the interpretability of our results, particularly in stratified analyses. Several cause-specific estimates may have also been biased downward due to "healthy worker" effects common with the use of general population reference rates. The primary strengths of this study include the use of multiple sources for vital status ascertainment and complete work history records of individuals ever-employed at the facilities for an extended period. The use of multiple vital status sources allowed for the verification of deceased status and improved the overall sensitivity of vital status follow-up throughout the full risk period of the study. The use of complete work history records precluded selection biases due to gaps in available data and included work history over a 21-year period during the earliest years of facility operation when exposures were estimated to be most intense. The cohort was followed for a mean of 33 years with sufficient time to observe mortality due to most causes of interest and without excessive influence from "healthy worker" effect related to recency of active employment.

5 | CONCLUSION

This investigation involved the enumeration of a novel cohort of UAW members employed at automotive electronics manufacturing facilities in Huntsville, Alabama between 1972 and 1993. Workers at the facilities reported exposure to industrial agents with known toxicity and carcinogenicity and results suggest they experienced greater all-cause mortality rates relative to other large UAW cohorts. The observed excesses of all-cause and cause specific mortality among pre-1977 hires are consistent with worker concerns over particularly adverse working conditions at the Plant 1 building. Among female workers, the observed excesses of mortality may indicate that women were more likely than men to hold non-skilled or non-salaried jobs with greater potential exposure to production processes. The study cohort experienced an elevated rate of mortality due to brain and nervous system cancers as well as nervous system disorders relative to the U.S. referent, which is consistent with previous studies of workers with occupational exposure to lead and chlorinated solvents. We observed evidence of asbestos exposure in the cohort, although the prevalence and source of this exposure is unknown. The relatively small size of the cohort led to imprecise estimates for some causes of a priori interest, which limited the interpretation of our findings. The observed mortality excesses warrant further investigation of hazards at the facilities using process-specific exposure information obtained from company sources. Limitations stemming from the reliance on mortality outcomes and low statistical power for malignant disease could be overcome through the ascertainment of cancer incidence using available residential history data and follow-up with state cancer surveillance registries.

AUTHORS' CONTRIBUTIONS

NDB collaborated with the UAW during the conception of the work, designed the study, acquired study data, conducted analyses, interpreted results, drafted the manuscript, had final approval of the published version, and is accountable for the integrity of the work. KK-R participated in the vital status follow-up and study analysis and provided revisions on the manuscript. DR participated in the design and analysis of the study and provided critical review of the manuscript. AK, WR, MT, and SM provided critical review of the study design, analysis, and interpretation of the work and contributed important revisions to the manuscript.

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The study was approved by the University of North Carolina at Chapel Hill Institutional Review Board.

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The authors report no conflicts of interest.

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Steven B. Markowitz declares that he has no conflict of interest in the review and publication design regarding this article.

DISCLAIMER

None.

ORCID

Nathan DeBono http://orcid.org/0000-0002-5087-107X
David Richardson http://orcid.org/0000-0001-8550-0212

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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