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Original Contribution

Metalworking Fluid Exposure and Stroke Mortality Among US Autoworkers

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Although air pollution is an important risk factor for stroke, few studies have considered the impact of workplace exposure to particulate matter (PM). We examined implications of exposure to PM composed of metalworking fluids (MWFs) for stroke mortality in the United Autoworkers–General Motors cohort. Cox proportional hazards models with age as the timescale were used to estimate the association of cumulative straight, soluble, and synthetic MWF exposure with stroke mortality, controlling for sex, race, plant, calendar year, and hire year. Among 38,553 autoworkers followed during 1941–1995, we identified 114 ischemic stroke deaths and 113 hemorrhagic stroke deaths. Overall stroke mortality risk was increased among workers in the middle exposure category for straight MWF (hazard ratio (HR) = 1.31, 95% confidence interval (CI): 0.87, 1.98) and workers in the highest exposure category for synthetic MWF (HR = 1.94, 95% CI: 1.13, 3.16) compared with workers who had no direct exposure. Ischemic stroke mortality risk was increased among workers in the highest exposure categories for straight MWF (HR = 1.45, 95% CI: 0.83, 2.52) and synthetic MWF (HR = 2.39, 95% CI: 1.39, 4.50). We observed no clear relationship between MWF exposure and hemorrhagic stroke mortality. Our results support a potentially important role for occupational PM exposures in stroke mortality and indicate the need for further studies of PM exposure and stroke in varied occupational settings.

hemorrhagic stroke; ischemic stroke; particulate matter; $PM_{2.5}$

Abbreviations: CI, confidence interval; HR, hazard ratio; PM, particulate matter; MWF, metalworking fluid.

An estimated 795,000 strokes occur each year in the United States (1). While global age-adjusted mortality rates for both ischemic and hemorrhagic strokes decreased from 1990 to 2015, the absolute numbers of people who have strokes annually, and associated morbidity, have increased (1–3). Data from the National Inpatient Sample indicates further that hospitalization rates for ischemic stroke increased significantly among working-age adults between 1995 and 2012 (4). While the majority of strokes can be attributable to modifiable risk factors including hypertension, obesity, smoking, sedentary lifestyle, and unhealthy diet, nearly one-third (29%) of stroke risk globally is attributed to air pollution (5).

Early studies identified increases in stroke mortality following episodes of acute air pollution, including the Great London Fog of 1952 (6, 7). Subsequent research consistently identified short-term increases in exposure to common pollutants as a risk factor for stroke (8–11), with stronger associations reported for recurrent stroke (12, 13) and in individuals with comorbid diabetes mellitus or cardiovascular risk factors (9, 10, 13). Long-term exposure to air pollution is also associated with higher risk of hospitalization for stroke and stroke mortality. In a random-effects meta-analysis of data from 11 European cohorts, long-term exposure to fine particles (i.e., particulate matter (PM) less than or equal to 2.5 μm in aerodynamic diameter ($PM_{2.5}$)) was associated with increased risk of hospital admission for stroke even at concentrations below current air quality limit values (14). Exposures to nitrogen dioxide, nitric oxide, carbon monoxide, and traffic density have also been linked with hospital admission for stroke (15–17). Prior research finds that living near a main road, traffic sources, point sources of emissions, and increased exposure to air pollutants, including fine particles, are associated with increased stroke mortality (15, 16, 18–22).

Whereas air pollution is acknowledged as an important global risk factor for stroke, very few studies have considered the impact of occupational exposure to PM for stroke. The present study examines occupational exposure to particulate matter mainly composed of metalworking fluids and stroke mortality in the United Autoworkers–General Motors cohort. The study data are composed of longitudinal work records combined with an extensive retrospective exposure assessment for an iconic cohort of Michigan autoworkers from 1941 through 1995 (23). Metalworking fluids (MWFs) are widely used in machining operations as coolants and lubricants. During grinding, cutting, and drilling, the fluid is heated and aerosolized, resulting in particles that may include metals and polycyclic aromatic hydrocarbons comparable to PM produced by fossil fuel combustion (24–27). The National Institute for Occupational Safety and Health estimated that 1.2 million workers were exposed to MWFs in the United States based on the National Occupational Exposure Survey (28) and use of water-based MWF is projected to increase both in the United States and globally over the next decade (29, 30). Our analysis leverages quantitative MWF exposure and linked vital statistics in order to examine the association between cumulative exposure to straight, soluble, and synthetic MWFs and cause-specific mortality for overall, ischemic, and hemorrhagic stroke in this cohort of American autoworkers.

METHODS

Study population

The United Autoworkers–General Motors cohort mortality study was originally designed to assess the health implications of occupational exposures for workers employed by General Motors (Detroit, Michigan) and has been described in detail previously (31, 32). The cohort includes all hourly workers identified through company records at 3 automobile manufacturing plants in Michigan. The study population is composed of workers hired between January 1, 1938, and December 31, 1984. Cohort eligibility was originally restricted to those employed for at least 3 years to minimize potential confounding introduced by short-term or transient workers (33). Follow-up began 3 years after hire and extended to date of death or December 31, 1995.

Exposure assessment

MWF is classified by composition into 3 broad types. Straight MWFs are mineral oil–based fluids, and soluble MWFs are oils emulsified in water. Synthetic MWFs are also water-based and contain chemical lubricants but no oil at all. Anticorrosive chemicals are added to improve performance, and biocides are added to the water-based fluids to reduce microbial contamination. Exposure to MWFs was estimated over time for each plant, department, and job based on 541 personal and area samples for particulate matter (mg/m^3) collected by industrial hygienists, in combination with company industrial hygiene records (23, 25).

Exposures were estimated by particle-size fraction and fluid type (straight, soluble, synthetic) and assigned for each combination of plant, department, job, and calendar year. Changes in exposures over time were based on scale factors developed for retrospective exposure estimation (23). For jobs with mixed exposures, assignment was based on the percentage of time each fluid type was used. Annual exposure to each type of fluid and size fraction was calculated for each subject by combining work histories with the estimated exposure concentrations. Subjects missing more than 50% of their work histories were excluded (less than 3% of the study population). Gaps in work histories for remaining individual subjects were interpolated based on their previous and subsequent jobs. Using these data, we created a time-varying sum of annual MWF exposure, taking into account the percentage of each year the subject actively worked. In all analyses, cumulative exposure was defined through the preceding the year of interest (i.e., lagged by 1 year). Because follow-up extends beyond employment termination to date-of-death or the end of the study period, cumulative exposure remains constant after leaving work.

We created categories of cumulative exposure for each MWF type with cutpoints defined in order to distribute cases evenly across categories. For straight and synthetic MWF, workers with no direct exposure to each respective fluid type comprised the referent. Due to the ubiquity of exposure to soluble fluids, the reference category was set at 0–0.05 mg/m^3-years, an order of magnitude below the National Institute for Occupational Safety and Health recommended exposure limit of 0.5 mg/m^3 per year (28).

Outcome measure

Our outcome of interest was cause-specific mortality attributed to overall stroke and, separately, to hemorrhagic stroke and ischemic stroke. Data on vital status were ascertained through the Social Security Administration, the National Death Index, plant records, and state mortality files. Cause of mortality was obtained from state vital records, death certificates, and the National Death Index. We defined ischemic stroke using codes 433 and 434 from the *International Classification of Diseases, Ninth Revision*, and defined hemorrhagic stroke using codes 431 and 432.

Covariates

Information on age, sex (male or female), race (Black, White, unknown), plant location (plant 1, plant 2, or plant 3), birth date, and year of hire was obtained through records provided by the employer. Year of hire was defined as categorical variables with tertiles serving as cutpoints. Calendar year was defined as a continuous variable and included in models as a penalized spline with degrees of freedom selected based on model fit using the Akaike information criterion (34).

Statistical analysis

Cox proportional hazards models with attained age as the timescale were used to model mortality risk attributed to all stroke, ischemic stroke, and hemorrhagic stroke as a function of cumulative exposure to straight, soluble, and synthetic fluids (35, 36). Cumulative exposures to each fluid type were defined as categorical variables in our primary analysis. To maximize statistical efficiency, cutpoints were based on the empirical distribution of the exposure among the cases. All statistical models included all 3 MWF types simultaneously and adjusted for sex, race, plant location, calendar year, and year of hire. Standard errors and 95% confidence intervals (CIs) were calculated using methods described by Rubin (37, 38). As a secondary analysis, MWF exposures were defined as continuous variables and included in models as penalized spline functions with degrees of freedom selected based on model fit. As sensitivity analyses, we created 3 alternative specifications of our main analysis. First, we defined calendar year and year of hire as categorical variables with 3 categories each; second, we defined both variables as linear terms; and third we defined both as continuous variables with penalized spline functions.

All analyses were conducted using R, version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria). This study was approved by the institutional review board at the University of California, Berkeley.

RESULTS

In total, 38,553 eligible workers were identified through company records. The majority were male and White. The median follow-up time was 26.0 years, and the median tenure was 14.9 years. The 3 types of MWF showed low to moderate correlation based on nonparametric Spearman ρ correlation statistics. For the majority of follow-up, workers had no exposure to MWF (57.8% of person-time) or were exposed to a single type of MWF (27.2% of person-time). In total, 114 deaths due to ischemic stroke and 113 deaths due to hemorrhagic stroke were identified over the study period. (Table 1) Across all 3 plants, levels of overall MWF exposure declined beginning in the early 1970s. These declines were most pronounced for the oil-based fluids: soluble MWF and straight MWF (Figure 1).

Cumulative exposure to straight MWF was associated with increased risk for overall stroke mortality for those in the middle (hazard ratio (HR) = 1.31, 95% CI: 0.87, 1.98) and highest (HR = 1.16, 95% CI: 0.79, 1.70) categories of exposure versus workers with no direct exposure to straight MWF. We observed no clear relationship between cumulative exposure to soluble MWF and overall stroke mortality risk. We observed consistently increased risk for overall stroke mortality for those in the lowest (HR = 1.85, 95% CI: 1.12, 3.07), middle (HR = 1.22, 95% CI: 0.73, 2.06), and highest (HR = 1.94, 95% CI: 1.19, 3.16) categories of synthetic exposure versus workers without direct exposure to synthetic MWF (Figure 2, Web Table 1, available at https://doi.org/10.1093/aje/kwac002).

For ischemic stroke mortality, cumulative exposure to straight MWF was associated with increased risk for those in the lowest (HR = 1.37, 95% CI: 0.77, 2.43), middle (HR = 1.48, 95% CI: 0.82, 2.68), and highest (HR = 1.45, 95% CI: 0.83, 2.52) categories of exposure versus workers with no direct exposure to straight MWF. We observed no clear relationship between exposure with soluble MWF. Exposure to synthetic MWF was associated with increased risk of ischemic stroke mortality for those in the middle (HR = 1.67, 95% CI: 0.93, 3.02) and highest (HR = 2.39, 95% CI: 1.33, 4.32) categories of exposure versus workers with no direct exposure to synthetic MWF. (Figure 3, Web Table 2) In our analysis of hemorrhagic stroke mortality, we found modestly increased risk among workers with the highest cumulative exposure for straight, soluble, and synthetic MWF. However, results for hemorrhagic stroke risk are imprecise as evidenced by wide confidence intervals (Figure 4, Web Table 3).

As a secondary analysis we treated cumulative exposures to MWF as continuous variables and used penalized splines to visualize the exposure-response relationship for overall stroke mortality and then for ischemic and hemorrhagic stroke mortality separately. For both overall stroke and ischemic stroke mortality, we observed an initial increase in risk with higher levels of exposure but an apparent inverse association at the highest exposure levels for straight MWF. Cumulative exposure to synthetic MWF was associated with increased risk of overall and ischemic stroke mortality at all exposure levels (Web Figures 1 and 2). Splined results for hemorrhagic stroke suggest only slightly increased risk associated with increased exposure to straight MWF (Web Figure 3). As a sensitivity analysis, we created 2 alternative specifications of our primary analysis. We observed only minor differences in estimates when calendar year and year of hire were alternatively specified as categorical or linear variables (Web Tables 4–6).

DISCUSSION

We leveraged quantitative exposure measures linked with vital statistics to examine the implication of cumulative exposure to MWFs for stroke mortality in a cohort of US autoworkers. Whereas past research consistently identifies ambient PM exposure as an important risk factor for stroke incidence and mortality worldwide, our results suggest a potentially important role for occupational PM exposures, which are known to differ from ambient exposures in their composition, frequency, and duration and are typically experienced at substantially higher levels (39). Careful examination of occupational PM exposure as a risk factor for stroke mortality is further motivated by the essential fact that workplace exposures can be carefully monitored and subjected to regulatory or voluntary exposure limits in order to protect worker health (28).

Few prior studies have considered the implications of occupational PM exposure for stroke risk, and the existing studies have produced conflicting results. In a prospective cohort study of 983,409 manual workers identified from the Swedish National Census, followed over 1987–2005, the incidence of ischemic stroke was increased among both men and women exposed to both small and large particles for at least 5 years as compared with those who were never exposed (40). The authors of this study did not additionally consider incidence of hemorrhagic stroke. By contrast, in

Table 1. Demographic Characteristics for the United Autoworkers–General Motors Cohort, Michigan, 1941–1995

Characteristic	Full Cohort (n = 38,553)			Overall Stroke (n = 232)			Ischemic Stroke (n = 114)			Hemorrhagic Stroke (n = 113)		
	No.	%	Median (IQR)	No.	%	Median (IQR)	No.	%	Median (IQR)	No.	%	Median (IQR)
Sex												
Male	33,796	88		215	93		102	89		113	96	
Female	4,757	12		17	7		12	11		5	4	
Race												
White	22,816	59		79	34		42	37		37	31	
Black	7,133	19		71	31		26	23		45	38	
Unknown	8,604	22		82	35		46	40		36	31	
Plant												
Plant 1	9,091	24		102	44		37	32		65	55	
Plant 2	17,090	44		96	41		59	52		37	31	
Plant 3	12,372	32		34	15		18	16		16	14	
Year of hire[a]			1996 (1953, 1974)			1950 (1946, 1953)			1949 (1946, 1953)			1951 (1946, 1955)
Tenure, years			14.9 (7.0, 26.3)			19.1 (10.4, 26.7)			16.9 (8.6, 27.0)			20.7 (10.7, 26.5)
Follow-up, years			25.2 (16.7, 34.3)			28.3 (20.0, 35.3			30.8 (20.8, 37.0)			26.1 (17.8, 32.5)
Cumulative exposure, mg/m^3/yr^2[b,c]												
Straight MWF			0.7 (0.2, 2.5)			1.3 (0.3, 3.0)			1.3 (0.3, 2.5)			1.3 (0.4, 3.7)
Synthetic MWF			4.9 (2.0, 12.3)			11.8 (4.4, 23.0)			10.8 (3.7, 20.2)			13.6 (5.3, 25.8)
Solid MWF			0.5 (0.2, 1.7)			1.2 (0.2, 3.0)			1.6 (0.3, 2.8)			0.7 (0.1, 3.1)

Abbreviation: IQR, interquartile range; MWF, metalworking fluid.

[a] For individuals employed at more than 1 plant over the follow-up, their designation was based on the site where they accrued the most work record time.

[b] Among ever-exposed individuals at the end of follow-up only. Exposures were lagged 1 year.

[c] Units of cumulative metalworking exposure are milligrams per meters cubed per year squared (mg/m^3/yr^2).

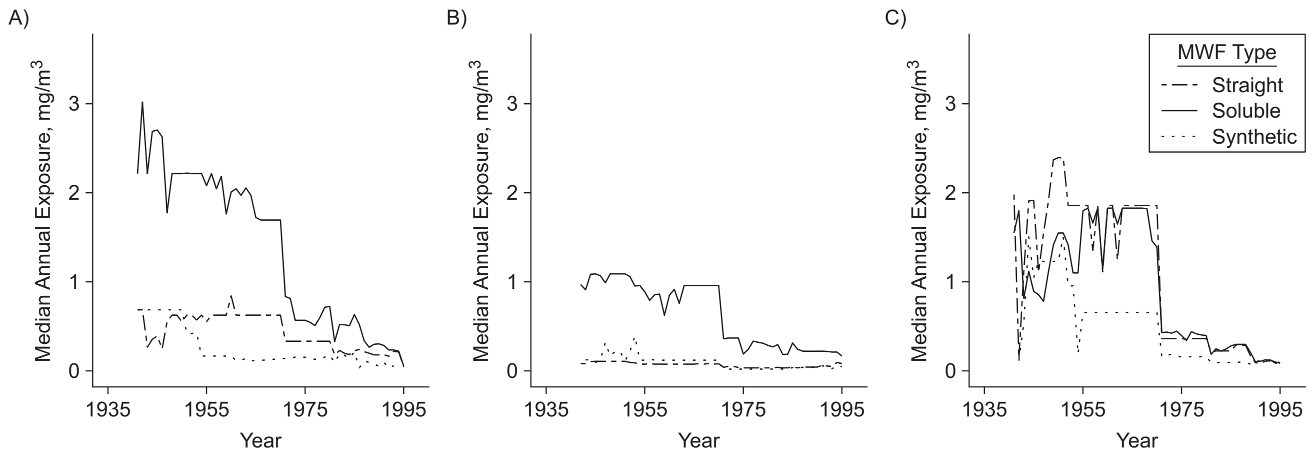

Figure 1. Median annual exposure to soluble, straight, and synthetic metalworking fluid (MWF) (mg/m^3) among the exposed according to which plant they worked in, Michigan, 1991–1994. A) Plant 1; B) plant 2; C) plant 3.

a second cohort study of Swedish male construction workers, occupational exposure to inorganic dust, wood dust, fumes, or gases and irritants was not associated with stroke (41), although the investigators did not distinguish between ischemic and hemorrhagic stroke and did not examine different types of exposures separately.

The present study examines the implication of cumulative exposure to 3 types of MWF for overall stroke mortality risk, ischemic stroke mortality risk, and hemorrhagic stroke mortality risk. Consistent with prior studies, we found the rate of hemorrhagic stroke mortality among Black workers to be approximately double that of White workers (42). Whereas hemorrhagic stroke deaths account for the minority of all stroke deaths in the US general population (43), throughout the study period we recorded 114 deaths due to ischemic stroke and 113 deaths due to hemorrhagic stroke. First, it is possible that some proportion of the hemorrhagic stroke deaths are secondary to trauma, given prior research that demonstrates high rates of fatal traumatic brain injury among workers engaged in physically demanding occupations (44). Second, our study period includes follow-up that precedes widespread use of computed tomography, in the late 1970s, before which it was difficult to differentiate ischemic and hemorrhagic stroke. Finally, we registered only

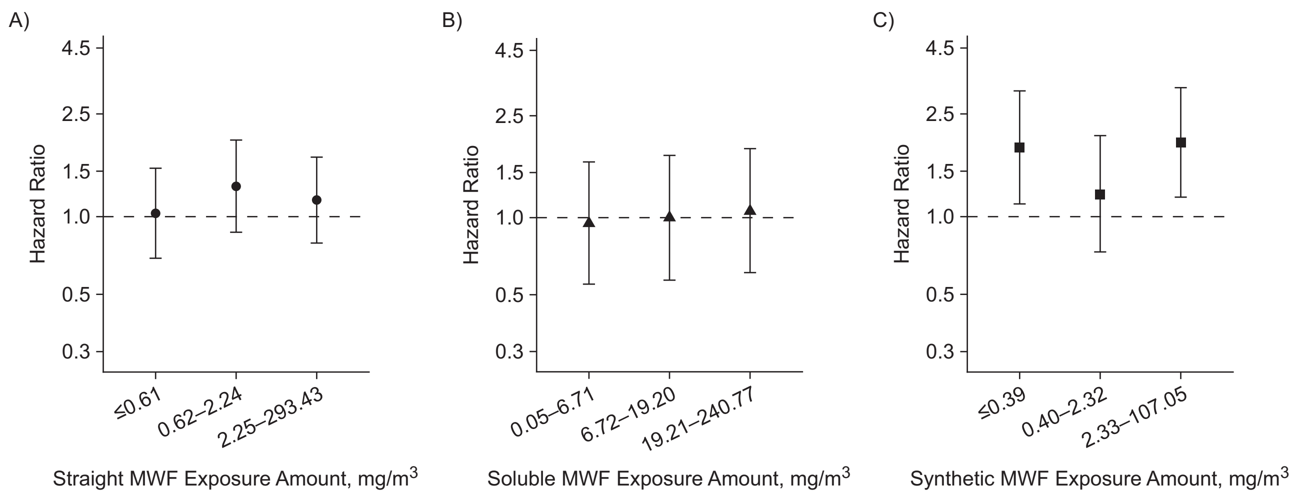

Figure 2. Hazard ratios for overall stroke mortality risk and cumulative exposure to straight (A), soluble (B), and synthetic (B) metalworking fluids (MWFs), Michigan, 1991–1994. Cox proportional hazards models with attained age as the timescale were used to model overall stroke mortality risk as a function of cumulative exposure to straight, soluble, and synthetic MWFs. Cumulative exposures for all MWFs were lagged by 1 year. To maximize statistical efficiency, cutpoints were based on the empirical distribution of the exposure among the cases. For straight and synthetic fluids, workers not exposed to the respective fluid type formed the reference category. Due to the ubiquity of exposure to soluble fluids, the reference category was set at 0–0.05 mg/m^3-years. All models adjusted for sex, race, plant location, calendar year, and year of hire.

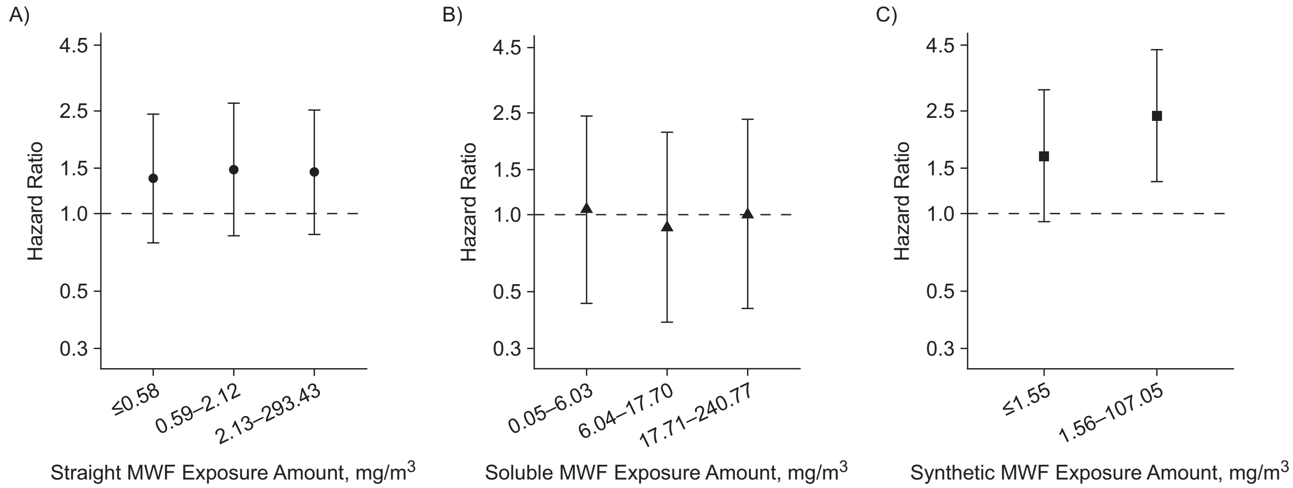

Figure 3. Hazard ratios for ischemic stroke mortality and cumulative exposure to straight (A), soluble (B), and synthetic (B) metalworking fluids (MWFs), Michigan, 1991–1994. Cox proportional hazards models with attained age as the timescale were used to model ischemic stroke mortality risk as a function of cumulative exposure to straight, soluble, and synthetic MWFs. Cumulative exposures for all MWFs were lagged by 1 year. To maximize statistical efficiency, cutpoints were based on the empirical distribution of the exposure among the cases. For straight and synthetic fluids, workers not exposed to the respective fluid type formed the reference category. Due to the ubiquity of exposure to soluble fluids, the reference category was set at 0–0.05 mg/m^3-years. All models adjusted for sex, race, plant location, calendar year, and year of hire.

227 total stroke deaths over the study period, which raises the possibility that the percentage of hemorrhagic stroke deaths reflects random chance.

For overall stroke risk, we observed the strongest associations with cumulative exposure to synthetic MWF, and for ischemic stroke risk, we observed the strongest associations with cumulative exposure to straight and synthetic MWF. Across analyses, we observed no evidence of an association between soluble MWF exposure and stroke risk. One potential explanation for the absence of an association between soluble MWF and stroke mortality is that differences in potency, composition, and use of MWF types are such that exposure to straight and synthetic MWF—but not soluble MWF—plays an etiological role in stroke mortality. Although there is substantial overlap in the composition of the 3 types of MWF (45, 46), previous studies have

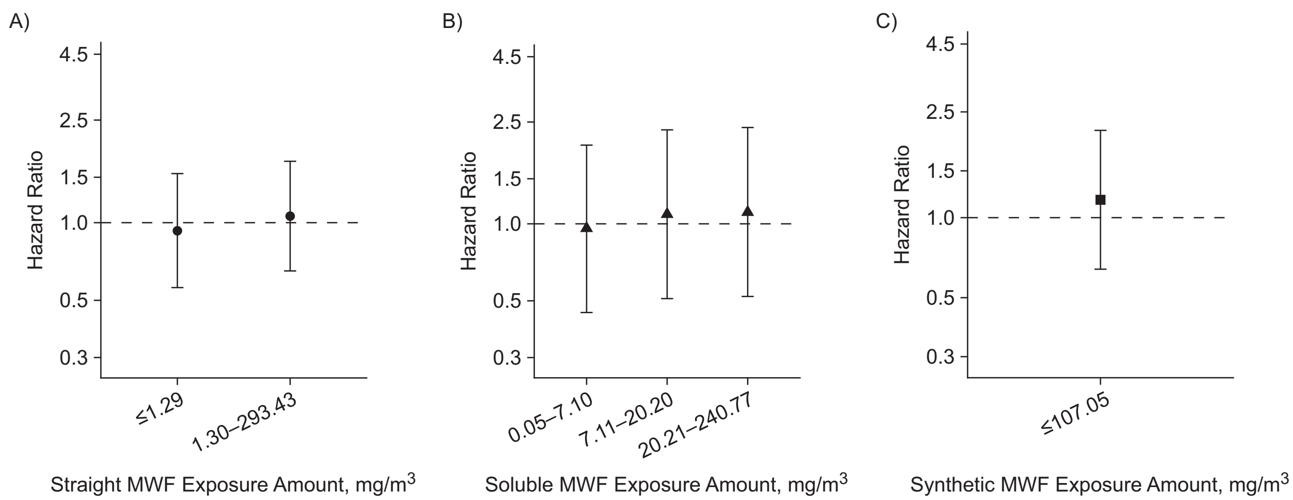

Figure 4. Hazard ratios for hemorrhagic stroke mortality and cumulative exposure to straight (A), soluble (B), and synthetic (B) metalworking fluids (MWFs), Michigan, 1991–1994. Cox proportional hazards models with attained age as the timescale were used to model hemorrhagic stroke mortality risk as a function of cumulative exposure to straight, soluble, and synthetic MWFs. Cumulative exposures for all MWFs were lagged by 1 year. To maximize statistical efficiency, cutpoints were based on the empirical distribution of the exposure among the cases. For straight and synthetic fluids, workers not exposed to the respective fluid type formed the reference category. Due to the ubiquity of exposure to soluble fluids, the reference category was set at 0–0.05 mg/m^3-years. All models adjusted for sex, race, plant location, calendar year, and year of hire.

demonstrated differences in cause-specific mortality risk associated with exposure to different MWF types. Studies using data from the United Autoworkers–General Motors cohort have demonstrated increased risk for cause-specific mortality due to bladder cancer, melanoma, and ischemic heart disease with greater cumulative exposure to straight MWF but not with soluble or synthetic MWF exposure (47–49). While collectively these results suggest that soluble MWF is associated with minimal stroke mortality risk, we note that estimates for soluble MWF are imprecise due to the very small number of cases with no direct exposure and greater variability in composition and use than other MWF types over the study period and therefore must be interpreted cautiously.

Within our study period, MWF exposure levels declined substantially beginning in the 1970s. This decline reflects considerable modifications across all 3 plants including installation of recirculating general air cleaners, enclosures, and local exhaust ventilation; improved filtration of recirculated air; renovation of old plant buildings; and increased use of synthetic MWFs (23). Declines in stroke mortality rates in the United States also accelerated beginning in the early 1970s (50), which has been attributed primarily to improved diagnosis and treatment of hypertension (51, 52). Coincident declines in both MWF exposure levels and stroke mortality in the general population raise the possibility that the apparent association between ischemic stroke mortality and MWF exposure are driven at least in part by secular trends. Confounding by secular trends in our analysis is limited by the fact that we controlled for both continuous calendar year and categorical year of hire. That we detect the strongest associations between ischemic stroke mortality and exposure to synthetic MWF—which was used far more frequently after 1970 as stroke mortality declined in the general population—further indicates that our results cannot be explained by secular trends alone.

Our findings linking cumulative exposure to MWF with increased risk for ischemic stroke mortality are consistent with prior research demonstrating increased risk of cardiovascular mortality risk associated with cumulative exposure to both straight and synthetic MWF in this study population (49, 53–55). This link is supported further by prior research that suggests that exposure to PM triggers prothrombotic physiologic changes that collectively increase risk for ischemic stroke (56, 57). These include systemic endothelial dysfunction leading to accelerated atherosclerosis, plaque formation, and rupture (58, 59); increased arterial blood pressures (16, 59, 60); vasoconstriction secondary to increased inflammatory processes and oxidative stress (61–64); and for the cerebral vasculature specifically, exposure to moderate elevations in fine PM concentrations that are known to increase cerebral vascular resistance combined with lower blood flow velocity (65). Prior research has also linked PM exposure with hemorrhagic stroke, wherein both hypertension and vasoconstriction lead to increased vulnerability of brain vessels to rupture through acute endothelial dysfunction (66–69). In the context of prior research that identifies plausible biologic mechanisms linking PM exposure with stroke and the robust epidemiologic literature on ambient PM exposure, the results for the present study should therefore motivate ongoing study of a potentially important role for occupational PM in stroke incidence and mortality.

Finally, although these analyses are based on a historical cohort, they have policy relevance and implications for present-day working populations. The current permissible exposure limit (PEL) established by the Occupational Safety and Health Administration (OSHA) for particulates not otherwise classified (PNOC)—which includes all MWFs other than oil mist—is 15 mg/m^3 (70). Although levels of MWF exposure for GM autoworkers decreased throughout the study period, an estimated 210 to 255 million gallons are used each year in the United States (71, 72). Further, the use of synthetic MWFs is projected to increase both in the United States and globally due to their superior machining performance (29, 30). Our analysis demonstrates increased stroke mortality risk at levels of exposure to synthetic MWF well below the OSHA PEL. Current exposure limits may therefore provide inadequate protection against stroke for workers with occupational MWF exposure, and our results further motivate careful consideration of new permissible exposure limits for occupational exposure to synthetic and semisynthetic MWF specifically.

Finally, whereas the United States still ranks among the world's largest automobile producers by volume, recent production statistics rank China, India, Brazil, and Mexico among the top 10 largest vehicle producers (73). In global settings such as these, ambient PM exposure is an established driver of stroke incidence and mortality, and workers are far less likely to be protected by regulatory limits for occupational exposure to MWF and other PM. Although findings from the present study are unlikely to reflect the specific circumstances of workplaces abroad, they should motivate careful examination of the joint implications of occupational and environmental particulate matter exposure for global stroke risk.

Limitations

A key limitation of the present study is that—while cause-specific mortality data were available—we were unable to examine the relationship between cumulative MWF exposure and stroke incidence. Other potentially important confounders that were not available for the present study included tobacco use, residential address, and other sociodemographic measures, such as income and educational attainment. However, previous analysis of this study population showed little variation in smoking prevalence by degree of MWF exposure, and further demonstrated a null exposure response between straight MWF and lung cancer, which argues against strong confounding by smoking (74). Data on race and ethnicity, which are known risk factors for stroke in the general population (75–77), is limited to "White" or "Black" in the present study, with race unknown for approximately 20% of the study population.

The study data lacked measures of comorbid illnesses that are known risk factors for stroke (i.e., hypertension, coronary artery disease, atrial fibrillation). Risk factors such as these may be important effect modifiers for the present analysis (78). They may also operate as time-dependent confounders if they are affected by prior MWF exposure and affect future exposure (through leaving work) as well as stroke mortality risk. This would result in a healthy-worker survivor effect, wherein healthier workers unaffected by comorbid illnesses remain employed and therefore accrue the greatest exposure over their lifetime (79–84). The results of the present study therefore may underestimate the true association between MWF and stroke mortality risk. This motivates the use of methods that can adequately address time-dependent confounding affected by prior exposure (i.e., g-methods), which should be implemented in future studies where time-varying measures of both occupational exposures and comorbid illness are available.

Exposure to MWF was estimated based on company records and samples collected by industrial hygienists, but we have no exposure data after employment termination. Cumulative exposure levels after leaving work may therefore underestimate true exposure to particulate matter, particularly for those who found employment in another automobile manufacturing setting after leaving these GM plants. Finally, it is important to note that while our results may generalize to stroke mortality risk among autoworkers employed by major automobile manufacturers in the Midwestern United States, they may not generalize to other manufacturing settings where differences in the composition of PM, industrial operations and practices, and timing, duration, and level of exposure may translate to meaningful differences in stroke mortality risk.

Conclusions

We leveraged quantitative exposure measures linked with vital statistics in order to examine the implication of cumulative exposure to MWFs for stroke mortality in the United Autoworkers–General Motors cohort. We found that cumulative exposures to both straight and synthetic MWF were associated with increased overall stroke mortality risk and ischemic stroke mortality risk. Whereas prior literature consistently identifies ambient PM exposure as an important global risk factor for stroke, our results motivate ongoing study of the implications of PM exposure for stroke incidence and mortality in varied occupational settings.

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