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Final Report

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NIOSH 5R01OH009939-10

Aim 1: Develop job exposure matrices (JEMs) for PM and selected chemicals based on job-level exposures rather than distinct exposure groups (DEGs), adjusting for respirator use.

- 1a: Develop and extend JEMs for TPM, coarse PM and PM2.5 based on job-level exposures.

We expanded the JEMs for PM to include additional jobs and DEGs. This involved the use of several data sources (some legacy databases) to incorporate information on time varying exposures with job histories from the database human resource (HR) files. Specifically, during the period from 1980 to 1998, many jobs within the industrial hygiene (IH) database were made obsolete or reorganized into differently named jobs. We also expanded the basic JEMs to include an additional facility.

We continued our efforts to match jobs from the IH database directly to jobs in the HR dataset across 11 facilities. At our test facility, we matched 95.7% of jobs in the HR database to the IH job description (583 out of 609 jobs, 26 un-matched). This represented 94.7% person-years at the facility (27,220 out of 28,725 person-years, 1505 person-years un-matched).

We created a crosswalk document between our jobs, DEGs, and the U.S. Department of Labor's O*NET occupational categories. This allowed us to extrapolate our exposure and psychosocial stress data to a larger subset of our cohort.

- 1b. Develop job-based JEMs for selected chemicals, including fluoride, metals, BaP, coal tar pitch (CTP), oil mist, silica, bauxite, and alumina.

We also did work to link IH and HR jobs (see aim 1a), which was necessary in order to apply the job-based JEM for chemicals to the cohort. We combined the 20+ PAH measures, accounting for different sampling methods and limits of detection. We developed a JEM for PAH exposure using a combination of 20+ PAH measures.

- 1c. Adjust the estimates of size-specific PM and chemical exposures for respirator use and efficacy (particle size, task-based, and individual-level corrections)

We developed JEMs to address PM2.5 and TPM exposure over time and with difference respirator use assumptions and job groupings. First, we expanded the time invariant TPM and PM2.5 JEMs to include respirator use assuming compliance and appropriate use in line with OSHA guidelines. This adjustment is based on perfect fit and consistent use. The second set of JEMs was adjusted for reasonable workplace use as determined by the published literature. In addition to time invariant respirator adjusted JEMs, we also incorporated time-varying information to each of the JEMS above.

At our 12 facilities, 2,881 (34%) reported using a respirator during the sampling. The vast majority of these 2,881 samples that reported respirator use were collected in the smelters, 2,527 (88%). A much higher proportion of samples collected in smelters reported respirator use than in fabrication: 46% vs 9%. Additionally, there is variability in respirator use over time (Figure below), with reported use beginning in the 1990s. The most common respirator adjustment was a 10-fold reduction in TPM, which was applied in 29% of all samples, 41% of smelter samples and 4% of fabrication samples. The mean unadjusted TPM across all samples was 5.91 mg/m3. Following application of the workplace respirator adjustment factor, the mean TPM was 2.46 mg/m3, a reduction of 3.45mg/m3 or 58%. This absolute large reduction is driven by the reduction of exposure in the smelters (8.48 to 3.42 mg/m3) rather than the fabrication units (0.82 to 0.49 mg/m3).

We accounted for time variance in exposures using a regression-based model and incorporated a respirator adjustment at the job level.

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Aim 2: Examine the impact of co-exposure to chemicals, physical stressors-noise and heat-and job stress as independent risk factors for IHD incidence, and as potential confounders, intermediates and effect modifiers of the cardiovascular effects of PM2.5 exposure among all active workers in aluminum smelters and fabrication facilities.

- The Occupational Information Network (O*NET) is a publicly available online network of occupational information developed by the US Department of Labor. Each occupation is linked to the Standard Occupational Classification (SOC) taxonomy. These occupational descriptors may be used to represent the average level of various job characteristics on a predefined ordinal scale. Recognizing the limitations of the job-demand survey, we mapped all PM2.5 cohort jobs to SOC codes to enable development of SOC-level metrics for physical demand, mental demand and exposures to temperature extremes.
- Rotational night work and hypertension: We extended our exposures to investigate the effects of rotational shiftwork, or work shifts that change according to a set schedule, on chronobiologic phase shifts and potentially related increases in hypertension risk. Our results suggest recent degree of rotational shiftwork exposure may be associated with higher rates of hypertension and rotational shiftwork may have an additional effect on hypertension risk not explained by night work.
- 2a. Exploiting ambient noise JEMs developed for other studies, as well as new measures of tympanic membrane exposure, add noise and its interaction with PM2.5 into acute and chronic effect models of IHD.

We generated additional long-term noise exposure metrics for further epidemiologic analyses of health outcomes, specifically anxiety, depression as well as cardiovascular outcomes. These long-term, exposure metrics will be defined by a cumulative noise exposure metric, and duration of exposure over above selected thresholds, 80 dBA, 85 dBA or 90 dBA.

- 2b. Take advantage of a recent job demand survey by examining effect modification of the PM2.5 and IHD relationship by heat exposure and job stress.

We extended work previously published by Tessier-Sherman et al in 2017 by augmenting the methods for evaluating noise exposure. We extended our analysis of the effect modification of heat in the relationship between PM2.5 and IHD by conducting a sensitivity analysis, comparing our own assessment of heat to that measured by job mapping via the O*Net database.

Aim 3: Explore the contribution of plant level, community and early life social and environmental characteristics to the incidence of cardiovascular disease.

We did work to include a greater number of workplace factors by creating JEMs (Aim 1) for standard occupational classes (SOCs).

Aim 4: Estimate the associations between cumulative exposure to PM2.5 (as well as the coarse particle fraction PM2.5-10) and longitudinal decline in pulmonary function.

- 4a. Address healthy worker survivor bias by restricting the analysis to subjects hired after start of follow-up (incident hires) and taking advantage of the extended follow-up to provide adequate power.
- 4b. Apply inverse proportional treatment weight (IPTW) to adjust for time varying confounding by health status (as measured by risk score) affected by prior exposure.

Analyses were completed using the parametric g-formula to assess the effect that hypothetical interventions on exposure to PM2.5 would have on FEV1 over age. The overall mean percent predicted FEV1 was 94% (median of 94.2% and an interquartile range of 84.7%, 103.7%). Results suggest a steeper relative decline at lower ranges of exposure (0-mg/m3), followed by a plateauing of the effect.

The observed percent predicted FEV1 (comparing the observed FEV1 measures to those predicted for this population based, with mean percent predicted at age 30 of 98.0% compared to 92.1% at age 60. Mean percent predicted values also increased under interventions on exposure reaching 94.3% at age 60 under an intervention of always unexposed, compared to the observed of 92.1%.

Aim 5: Examine the relationships between cumulative exposure to PM2.5, chemicals and COPD and CVD mortality, taking account of health status (risk score while actively employed) and new information on health status at age 65 (after leaving work) derived from linked Medicare claims files.

- 5a. Stratify by sex to address specifically the question of sex differences in the chronic response to exposures.

We have summarized preliminary results from previous mortality data from 1996-2011. This revealed 194 of 1,196 deaths related to IHD (Male=188). Twenty-nine deaths were associated with COPD. Cox models were run on this preliminary data, adjusting for age, sex, race, process type, job grade, previous hire, smoking, and BMI. Results indicate that exposure to 7.36-37.90 mg/m3-yr is associated with increased mortality due to IHD (7.36-15.88 mg/m3-yr: 1.21, CI 95% 0.75,1.94; 15.88-37.90 mg/m3-yr: 1.54, CI 95% 0.93, 2.53).

- 5b. Address HWSE by applying g-estimation.

We have made progress on addressing HWSE when examining the relationship between PM2.5 and CVD mortality. We estimated counterfactual risk of ischemic heart disease (IHD) mortality under hypothetical interventions to limit concentrations of annual PM2.5 exposure on 15,579 workers at nine facilities from 1998-2013. We applied the parametric g-formula, an approach that addresses healthy worker survivor bias by correctly adjusting for time-varying confounding affected by prior exposure. There were 123 observed IHD deaths in this relatively young cohort, with the oldest IHD death occurring at age 73. The risk ratio comparing the cumulative mortality risk under a hypothetical scenario in which annual exposure to PM2.5 was never higher than 200 µg/m3, the median annual exposure in this population, to the risk under observed exposures was 0.95 (95% CI 0.85, 1.05). Lowering the hypothetical limit to 50 µg/m3, approximately the 10th percentile of annual exposure, resulted in a risk ratio of 0.92 (95% CI 0.76, 1.11). Our findings to date are consistent with the hypothesis that interventions to reduce PM2.5 in occupational settings would reduce IHD mortality risk.