Metalworking fluids (MWF) are complex chemical mixtures used to lubricate and cool machinery during manufacturing processes. Early MWF were simple oils or combinations of oils, but by the mid 20th century, these straight MWFs ceded a large portion of their market share to soluble MWFs. Soluble MWFs are water-oil emulsions including diverse additives to preserve emulsification, prevent rust and microbial growth, and improve performance under high heat and pressure. By the 1970s, semisynthetic and synthetic MWF, which contain little to no oil, overtook straight oils in market share. However, soluble MWFs continue to have the largest share of the MWF market (Childers 2006).

Carcinogenicity of MWFs has been of concern as early as the 1970s, when the International Agency for Research on Cancer (IARC) classified mineral oils as a carcinogen, citing studies of occupational exposures among workers in oil, textile, and metal industries (*IARC monographs on the evaluation of carcinogenic risk of the chemical to man* 1973). In addition to mineral oil, soluble MWFs may also contain chromates, cycloalkanes, phenolic compounds, organochlorines, nitrosamines, and triazines—substances linked to cancer risk. Here, we assess the effect of exposure to soluble MWF on incidence of non-Hodgkin lymphoma (NHL).

* More on composition of the different fluids and putative biologic mechanisms

Incidence of NHL in the US has nearly quadrupled since 1960, but known risk factors have failed to account for this dramatic rise (Ekström-Smedby 2006). Some have attributed this rise to environmental and occupational exposure to organochlorides starting in the 1930s and peaking in the 1970s (Nelson 2005). However, the epidemiologic evidence linking NHL to occupational exposures remains weak (Alexander et al. 2007; Ekström-Smedby 2006). Two significant limitations faced by previous studies are the lack of quantitative exposure information and failure to control for the health worker survivor effect (HWSE). The HWSE is a dynamic selection process by which healthier individuals remain at work where they accumulate more exposure, and less healthy individuals leave work, thereby accruing less exposure (Arrighi and Hertz-Picciotto 1994). Standard analyses of longitudinal cohorts affected by the HWSE result in a downward bias the exposure-outcome associations of interest.

In the present analysis of the United Auto Workers-General Motors Cohort, we leveraged the quantitative metalworking fluid exposure data in tandem with employment data to control for the HWSE using two novel estimators capable of controlling for time-varying confounders affected by prior exposure: (1) the hazard-extended parametric g-formula (Wen et al. 2020) and (2) the sequentially doubly robust estimator for longitudinal modified treatment policies (Díaz et al. 2020). We compare the results from these two methods to results from a standard Cox proportional hazards analysis.

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