

# ILMA 2017 Annual Meeting MWF Committee

## MWF Studies on Autoworkers

John K. Howell, Ph.D., GHS Resources Inc.

## Papers Reviewed – 2017 Management Forum

- Shrestha, D., Liu, S., Hammond, S.K., LaValley, M., Weiner, D., Eisen, E. and Applebaum, K, “Risk of renal cell carcinoma following exposure to metalworking fluids among autoworkers,” *Occup Environ Med.*, **73** (10), 656-662 (2016)
- Picciotto, S., Ljungman, P. and Eisen, E., “Straight Metalworking Fluids and All-Cause and Cardiovascular Mortality Analyzed by Using G-Estimation of an Accelerated Failure Time Model with Quantitative Exposure: Methods and Interpretations,” *Amer J Epidemiology*, **183**(7), 680-688 (2016)

## Papers Reviewed – 2017 Management Forum

- Picciotto, S., Peters, A. and Eisen, S., “Hypothetical Exposure Limits for Oil-Based Metalworking Fluids and Cardiovascular Mortality in a Cohort of Autoworkers: Structural Accelerated Failure Time Models in a Public Health Framework,” *Amer J Epidemiology*, **181**(8), 563-570 (2015)
- Garcia, E., Picciotto, S., Costello, S., Bradshaw, P. and Eisen, E., “Assessment of the healthy worker survivor effect in cancer studies of the United Autoworkers-General Motors cohort,” *Occup Environ Med*, **74**, 294-300 (2017)



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F+L Articles > Quarter Three 2017 > Understanding the impact of metalworking fluids' exposure on workers' health

## UNDERSTANDING THE IMPACT OF METALWORKING FLUIDS' EXPOSURE ON WORKERS' HEALTH



In trying to set or guide policies, the U.S. Environmental Protection Agency (EPA), Occupational Health and Safety Administration (OSHA) and National Institute for Occupational Safety and Health (NIOSH) take into account scientific findings based on research which are usually published in peer reviewed journals. However, for the average person, epidemiology and statistics are vague or sometimes even unknown concepts. Thus, we depend on researchers and academicians to establish the relationship between exposure and disease.

During the Independent Lubricant Manufacturers Association (ILMA) Management Forum in April, John Howell, president of GHS Resources Inc., led the discussion on the health effects of metalworking fluids (MWF) on workers. Howell reviewed several studies by Picciotto and associates, using a relatively new sophisticated statistical method called g-estimation.

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**NEW ARTICLES**

# Papers Reviewed – 2017 Annual Meeting

- Brown, D., Picciotto, S., Costello, S., Neophytou, A., Izano, M., Ferguson, J. and Eisen, E., “The Healthy Worker Survivor Effect: Target Parameters and Target Populations,” *Curr Envir Health Rpt*, **4**, 364-372 (2017)
- Erika Garcia, Ph.D. Thesis, University of California, Berkeley, 2017
- Garcia, E., Bradshaw, P. and Eisen, E., “Breast Cancer Incidence and Metalworking Fluid Exposure in a Cohort of Female Workers,” *Amer J Epidemiology*, (Published on line, August 23<sup>rd</sup>, 2017)
- Chevrier, J., Picciotto, S. and Eisen, E., “A Comparison of Standard Methods With G-estimation of Accelerated Time Failure Models to Address The Healthy-worker Survivor Effect: Application in a Cohort of Autoworkers Exposed to Metalworking Fluids,” *Epidemiology*, **23**, 212-219 (2012)

# Brown, et al., Healthy Worker Survivor Effect

- In-depth review of time-varying confounding and selection bias mechanisms that give rise to healthy worker survivor effect (HWSE)
  - Ten papers on target populations reviewed: aluminum smelter and fabrication workers (4), autoworkers (2), copper smelter workers (1), iron ore miners (1) and uranium miners (1)
  - Papers include four estimation methods: inverse probability weighting, targeted maximum likelihood estimation, Cox proportional estimation model, G-estimation model
  - Authors conclude that “each of the estimation methods...offers the ability to control for...HWSE” and that “G-estimation also offers the ability to use follow-up time after leaving work, but has thus far been applied with a limited class of models”

# Erika Garcia Ph.D. Thesis

- “Occupational exposure to Metalworking Fluids and Incidence of Cancer in the United Autoworkers – General Motors Cohort: Assessing and Accounting for the Healthy Worker Survivor Effect”
  - Chapter 1: assessment of presence of HWSE in cancer studies in UAW-GM cohort
  - Chapter 2: exposure response relationship between cumulative MWF exposure and breast cancer among female workers: results suggest increasing exposure response curve for straight fluids and breast cancer (4,503 female workers; 21 total incident breast cancer cases)

# Erika Garcia Ph.D. Thesis

- “Occupational exposure to Metalworking Fluids and Incidence of Cancer in the United Autoworkers – General Motors Cohort: Assessing and Accounting for the Healthy Worker Survivor Effect”
  - Chapter 3: relationship between lung cancer mortality and exposure to straight and synthetic MWF. Using parametric g-formula, results showed slightly elevated lung cancer mortality related to straight MWF exposure, albeit with wide confidence levels. For synthetic fluids, biocide in the fluids, a marker for release of endotoxin, was associated with decreased lung cancer.

# Garcia, et al., Breast Cancer and Metalworking Fluid Exposure

- Cohort of 4,503 female hourly workers exposed to all types of MWF
- Cox proportional hazards models used to estimate hazard ratios (HR) for incident breast cancer (follow-up 1985-2013) and cumulative exposure (20-year lag) to straight mineral oils and to water-based soluble and synthetic MWF. Account state cancer registry began decades after cohort defined, analysis restricted to sub-cohorts hired closer to start of follow-up
- Among those hired after 1969, HR associated with a one interquartile range increase in straight MWF exposure was 1.13 (95%: 1.03-1.23)
- For premenopausal breast cancer, HR was elevated for exposure to synthetic MWF.

# Chevrier, et al., G-estimation and HWSE: Application to UAW-GM Cohort

- Compare results from Cox estimation models and g-estimation methods in 38,747 workers exposed to straight MWF for mortality from all causes, cancers, ischemic heart disease and COPD
- In standard models, HRs were elevated for cancers of larynx, prostate and rectum, but below or equal to 1.0 for all other outcomes

# Chevrier, et al., G-estimation and HWSE: Application to UAW-GM Cohort

- Adjustment for HWSE itself did not substantially change hazard ratios but g-estimation yielded higher HRs than standard Cox models for most outcomes. Exposures was related to increased risks of mortality from:
  - All causes combined
  - Heart disease
  - COPD
  - All cancers
  - Lung and prostate cancers
- Conclusion: G-estimation may provide a better control for HWSE than standard methods



## Renal disease kidney cancer and metalworking fluid exposure in autoworkers

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Abstract

Millions of workers in the U.S. are exposed to suspected nephrotoxins and carcinogens, yet epidemiologic studies of occupational kidney disease and kidney cancer are challenged by low power and poor exposure assessment. Metalworking fluids (MWFs), which are used to lubricate and cool metal during cutting and grinding processes, are among the widely used industrial exposures which may have adverse consequences for the kidney. MWFs consisting of straight mineral oils (also called straight MWFs) are a source of polycyclic aromatic hydrocarbons (PAHs). PAHs in general and MWFs in particular have been associated with other cancers, but inconsistent results have been reported for kidney disease and kidney cancer in occupational settings. The General Motors-United Autoworker (GM-UAW) cohort study provides an opportunity to overcome the main barriers of previous occupational studies in examining the association between MWFs and kidney outcomes due to its large size (over 46,000 subjects), over 60 years of follow-up, and quantitative exposure estimates of different types of MWFs, including straight MWFs. Further, we have available records of other potentially harmful occupational exposures in the GM-UAW plants which may be confounders. Therefore, to investigate the association between MWFs, kidney cancer, and end-stage renal disease (ESRD), the preferred outcome of PAH-induced kidney disease, we will: 1) conduct an industrial hygiene review to characterize any other occupational exposures (other than MWFs) in the GM-UAW cohort in order to better control for confounding; 2) determine the relationship between straight MWFs and kidney cancer incidence; and 3) estimate the dose-response relationship between straight MWFs and ESRD. We will also analyze subtypes of kidney cancer and ESRD, which may be important in reducing disease misclassification and providing better estimates of the