The Diesel Exhaust in Miners Study

applying the parametric G-formula to evaluate interventions for occupational risk assessment

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- Re-analyze Diesel Exhaust in Miners Study for risk of lung cancer accounting for healthy worker effect

- Data agreement with NCI/NIOSH

The Diesel Exhaust in Miners Study (DEMS)

- Cohort of 12,315 blue collar job workers from eight non-metal mining facilities
  (our analyses restricted to 8,307 "ever-underground" workers)

- Follow-up began at dieselization for each mine
  (1947-1967)

- Administrative end on December 31st 1997
  (Maximum follow-up 50 years)

DEMS

- Facilities selected to be low in other potential risk factors for lung cancer
  - radon, asbestos and silica

- Diesel Exposure and Lung Cancer Mortality (respirable elemental carbon as surrogate)

DEMS

- Earlier studies show associations between diesel exhaust exposures and lung cancer in this population (Attfield et al. 2011, Silverman et al. 2011)

- Important findings leading to IARC decision to classify diesel exhaust as a human carcinogen

- Meta-analysis results suggest excess lung cancer risk even at lower ranges of exposure (Vermeulen et al. 2014)

What is HWSE

- ▶ Healthy workers accumulate more exposure
  - ▶ Less healthy workers may
    - ▶ take more time-off
    - ▶ transfer to less exposed jobs
    - ▶ terminate employment earlier

- ▶ Potential health effects of exposure may be hidden or stronger than estimated

Traditional Solutions

- Employment status (or duration of work) affects the association between cumulative exposure and potential health effects

- If exposure does not cause termination of employment then duration of work can be treated as traditional confounder in studies looking at the effect of cumulative exposures.

- Steenland et al (1996) simulation study showed that conventional methods to remove HWSE bias fail if exposure increases the probability of leaving work

Exposure and Duration of Work

- We fit an accelerated failure time model to assess whether exposure affects time to termination of employment

- Interested in whether exposure makes workers leave work earlier ('accelerates' retirement)

Exposure and Duration of Work

- Time to termination of employment 33% shorter for every IQR increase in exposure (167 $\mu g/m^3$)

Table: Hazard Ratio (HR) approximations and 95% CIs, for termination of employment and IQR increase in REC exposure

Cohort Subset	HR (95% CI)
Ever-underground subcohort (n=8,307)	1.57 (1.47 - 1.62)
Incident hires only (n=7,750)	1.54 (1.44 - 1.60)
Incident hires and $\geq$3 years tenure (n=5,993)	1.33 (1.26 - 1.40)
Incident hires and $\geq$5 years tenure (n=4,971)	1.24 (1.17 - 1.30)

Advanced methods

- ▶ Group of methods collectively referred to as g-methods
  - ▶ G-estimation of Structural Nested Models
  - ▶ Marginal Structural Models and Inverse Probability Weights
  - ▶ G-formula

- ▶ Can adequately control for time varying confounding affected by previous exposure

Assess Lung Cancer under Hypothetical Interventions

- ▶ Hypothetical Intervention Levels
    - ▶ MSHA old limit of 400 $\mu g/m^3$ of total carbon (TC), and new limit of 160 $\mu g/m^3$ TC

    - ▶ ACGIH recommendations of 50 and 20 $\mu g/m^3$ elemental carbon (EC)

- ▶ We use internal study-specific exposure assessment relationships (Vermeulen et al., 2010) to convert TC values to EC and then from the submicron size fraction to the respirable fraction

Person-Time by Intervention

Table: Person-Time in the DEMS ever-underground subcohort affected under each intervention assessed

Intervention	% Active person-time above intervention
REC $\leq$260 $\mu g/m^3$ (MSHA, old)	10
REC $\leq$106 $\mu g/m^3$ (MSHA, new)	39
REC $\leq$65 $\mu g/m^3$ (ACGIH, old)	53
REC $\leq$25 $\mu g/m^3$ (ACGIH, new)	63

Estimates of Risk and Risk Ratios

Table: Cumulative incidence for lung cancer mortality and corresponding Risk Ratios (RR) and 95% CIs, under several interventions in the DEMS underground cohort

Intervention	Lifetime Risk (%)	RR (95% CI)
Observed Data	7.79	.
REC $\leq$260 $\mu g/m^3$ (MSHA, old)	7.77	0.99 (0.92 - 1.02)
REC $\leq$106 $\mu g/m^3$ (MSHA, new)	7.14	0.92 (0.64 - 1.15)
REC $\leq$65 $\mu g/m^3$ (ACGIH, old)	6.80	0.87 (0.57 - 1.15)
REC $\leq$25 $\mu g/m^3$ (ACGIH, new)	6.18	0.79 (0.47 - 1.13)

Conclusions

- Evidence of HWSE in the DEMS ever-underground subcohort

- Risk assessment: Assess intervention effects directly in the population of interest using the g-formula

- Lung Cancer risk reduction associated with increasingly more stringent diesel exhaust interventions in DEMS

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