Occupational exposure to PM & CVD

Sadie Costello, PhD
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Heart disease understudied in occupational studies
  ◦ Work–related risk factors for CVD
    • Job demand/control, heat, shift work, PM

Analyses from several cohorts
  ◦ Cohorts designed to study cancer
  ◦ Also small studies for short term outcomes

Statistical methods advancement
  ◦ Healthy worker survivor effect
What does occupational epi add?

- A really big exposure range
  - An order of magnitude higher than ambient

- Long-term exposure to PM
  - Large study

- A well-defined population
  - Large studies: no recruitment, records-based
Occupational traffic exposure
Highway patrol officers

• 9 male highway patrol officers

• In-vehicle exposures, four shift

• Cardiac & blood markers 10 & 15 hours after shift

• Inflammatory and coagulation markers associated with speed-change pollutants

Riediker M Cardiovascular Effects of Fine Particulate Matter Components in Highway Patrol Officers, Inhalation Toxicology, 2007 vol: 19 (sup1) pp: 99–105
Truckers

- 54,000 US trucking company workers (Garshik, PI)
- 15 years of follow up
- drivers & trucking terminals workers
- 2011 & 2014 papers reporting associations between duration of work associated with IHD mortality
  - Especially after adjustment for healthy worker survivor effect.


Neophytou, AM et al, A structural approach to address the healthy−worker survivor effect in occupational cohorts: an application in the trucking industry cohort. Occupational and environmental medicine, 2014 71(6), 442–447.
Miners

- Diesel Exhaust in Miners Study (DEMS); NCI & NIOSH

- 12,315 workers, eight non-metal mining facilities (30–50 years of follow up)

- Respirable PM
  - Mean underground = 1.9 mg/m³

- 2 papers in progress, diesel exhaust and PM increase risk of IHD mortality after adjustment for healthy worker survivor effect
Firefighters, boilermakers, smelting
Firefighters

- High risk of CVD
- Especially acute MI
- Heat, dehydration, adrenaline

- Controlled human exposure studies

- 10 participants

- Exposed to wood smoke, treadmill

- Inflammation biomarkers

- Increased inflammation and oxidative stress markers

Boilermakers

- 72 male boilermakers, panel study (Christiani, PI)
- Personal, real time PM$_{2.5}$ exposures
- Ambulatory ECG
- Increased odds of experiencing ventricular ectopy for every 100ug/m$^3$ increase in PM$_{2.5}$

Aluminum smelter workers

- 5,500 aluminum smelter workers (Cullen, PI)
- 15 years of follow up
- PM$_{2.5}$ JEM: records and measurements
- Health insurance claims
- A lot of covariate data
- Actively employed person time
- Increased risk of incident IHD after adjustment for healthy worker survivor effect

Costello et al/JESEE 2014
Neophytou et al AJE 2014
Brown et al Epidemiology 2015
Costello et al AJE 2016
Metalworking fluids
United Autoworkers – General Motors

- 40,000 autoworkers (Eisen, PI)
- 50 years of follow up
- JEM for respirable PM from 3 types of metalworking fluid
- Increased risk of IHD (and other CVD) mortality, stronger after adjusting for the healthy worker survivor effect

Chevrier et al Epidemiol. 2012
Costello et al AJIM 2013
Picciotto et al OEM 2013
Costello et al OEM 2015
Picciotto et al AJE 2015
Picciotto et al AJE 2016
Aluminum fabrication workers

- 8,000 aluminum fabrication workers (Cullen, PI)
- 15 years of follow up
- PM$_{2.5}$ JEM: records and measurements
- Health insurance claims
- A lot of covariate data
- Actively employed person time
- Current exposure increases risk of incident IHD. Cumulative exposure does too, after adjustment for HWSE.

Costello et al JESEE 2014
Neophytou et al AJE 2014
Brown et al Epidemiology 2015
Costello et al AJE 2016
Coal and silica
Coal Miners

- MSHA/NIOSH
- 9,000 underground coal miners
- National Study of Coal Workers’ Pneumoconiosis
- Increased risk of IHD mortality
  - Especially in Western and Eastern Appalachia

Silica

• SMR <1.00

• 74,000 Chinese miners and pottery workers, increased risk of CVD and IHD (Chen et al PLoS Med. 2012)

• 1,000 granite workers, 2-fold increase in IHD (Koskela et al OEM 2005)

• Reanalysis of 2,500 diatomaceous earth workers (Checkoway, PI)
Healthy Workers

- Very high exposures to PM
  - Different sources
- Exposure to other risk factors for CVD
  - heat, dehydration, lifestyle
- But, Healthy!
  - Physically strong
  - Fitness testing
    - Hire and throughout
  - Healthier than the general population
    - SMR < 1.00
Healthy Worker Survivor Effect

- Healthier workers accrue more exposure

- Less healthy workers
  - Take more time off
  - Transfer to jobs with less exposure
  - Leave work

- Looks like more exposure is good for workers!

- Especially for Heart Disease
Healthy Worker Survivor Effect

PM_{time 1} → Health Status → PM_{time 2} → Cumulative PM Exposure → CVD

?
G–methods

- G–estimation, g–computation, IPTW, TMLE
- Handle time–varying confounding affected by prior exposure
- Grounded in counterfactual framework
- Binary exposure
- Intervention interpretation
When does follow up start?

- “Target Trial” (Hernan, 2016)
  - Ideally
    - Factory doors open
    - Start exposure assessment
    - Start outcome assessment
- Reality
  - All workers employed
    - At a moment in time
  - Retrospective exposure
  - Prospective (retro) outcome
- What kind of workers are in cohort?
  - Already didn’t leave (or die!) from exposure

“left truncation bias”

Follow up time

PM_{time 1} → Health Status → PM_{time 2} → CVD
2 time points, 2 solutions

- HWSE mechanism can happen
  - Before follow up
    - Left truncation bias
  - During follow up
    - HWSE

- Left truncation bias
  - Restrict analysis to workers hired after the start of follow up

- HWSE
  - G–method
  - Need measured data on health status/leaving work
Applications

- Cohort restriction in Aluminum fabrication workers
  - Left truncation

- G-estimation in autoworkers
  - HWSE

- IPTW in Aluminum fabrication and smelting processes
  - HWSE
Fabrication cohort by years hired prior to follow up

<table>
<thead>
<tr>
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<th>Fabrication</th>
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<tbody>
<tr>
<td></td>
<td>Full Cohort</td>
<td>≤ 25 years</td>
<td>≤ 10 years</td>
<td>0 years</td>
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<tr>
<td>No. Subjects</td>
<td>7,805</td>
<td>7,759</td>
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<td>No. Cases</td>
<td>554</td>
<td>550</td>
<td>270</td>
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<tr>
<td>Male (%)</td>
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<td>White (%)</td>
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<tr>
<td>IHD age</td>
<td>53</td>
<td>53</td>
<td>51</td>
<td>50</td>
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</table>
Fabrication cohort

Hazard Ratio for IHD

Cumulative PM$_{2.5}$ (mg/m$^3$-years)

- 0 yrs
- ≤ 10 yrs
- ≤ 25 yrs
- Full
G-estimation v traditional Cox
Exposure to straight metalworking fluid

Chevrier J,
Epidemiology 2012
Cox MSM vs Traditional Cox: HR for Ischemic Heart Disease if always exposed above vs below 10th percentile of PM$_{2.5}$
Conclusions

- Progress in occupational PM & CVD

- Not easy to detect occupational PM & CVD
  - HWSE = harder analysis
    - May explain dearth of studies

- Apply the methods to occupational risk factors for CVD