Internal Validity of Air Pollution Assessment Methods: A tool for Evaluating Risk of Bias

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Study Objective

To develop and demonstrate the application of a tool to evaluate potential risk of bias (internal validity) of air pollution exposure assessment methods.

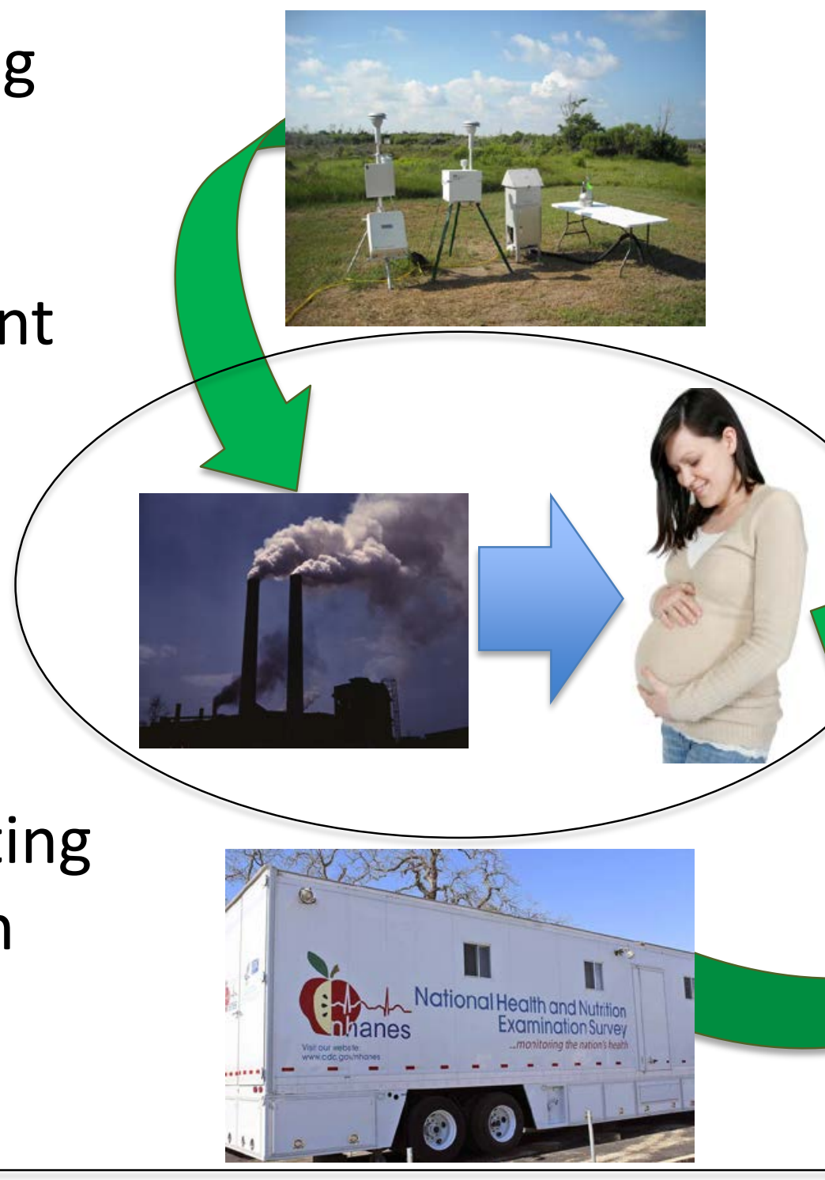
Background

Air pollution is a serious public health issue. As systematic review methods gain traction in environmental health to address relevant public health exposures of concern, such as air pollution, the need arises to develop appropriate tools to evaluate the accuracy of exposure assessment methods utilized in human epidemiology studies, such as those to measure air pollution.

Methods

We modified an existing tool for evaluating potential risk of bias of general exposure assessment methods, tailored for air pollution assessment. Exposure assessment metrics (i.e., modeling, monitoring, biomarkers) were evaluated separately.

We applied the tool to a proof of concept case studies using the Navigation Guide systematic review methodology investigating associations between general air pollution and Autism Spectrum Disorder (ASD).



We screened 1,158 references and identified 23 human studies that met our inclusion criteria. Two independent raters evaluated each study using the modified air pollution risk of bias tool.

We rated each chemical air pollutant separately by exposure assessment metric (i.e., monitoring, modeling, occupational job). After reaching consensus between the two reviewers, each rating and justification was recorded.

RISK OF BIAS

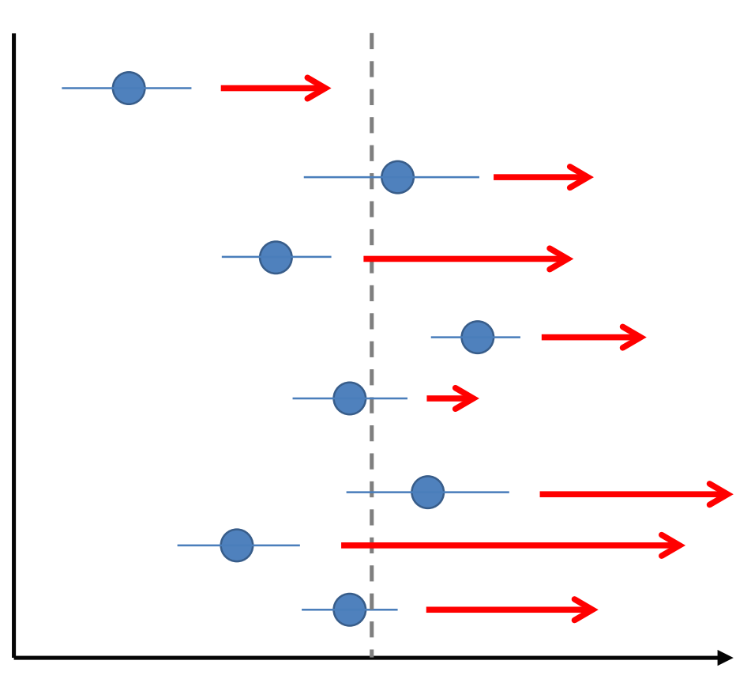
A measure of whether the design/conduct of a study alters the effect estimate or compromises the credibility of the reported association (or lack thereof) between exposure and outcome

Cochrane & AHRQ →

DOMAINS

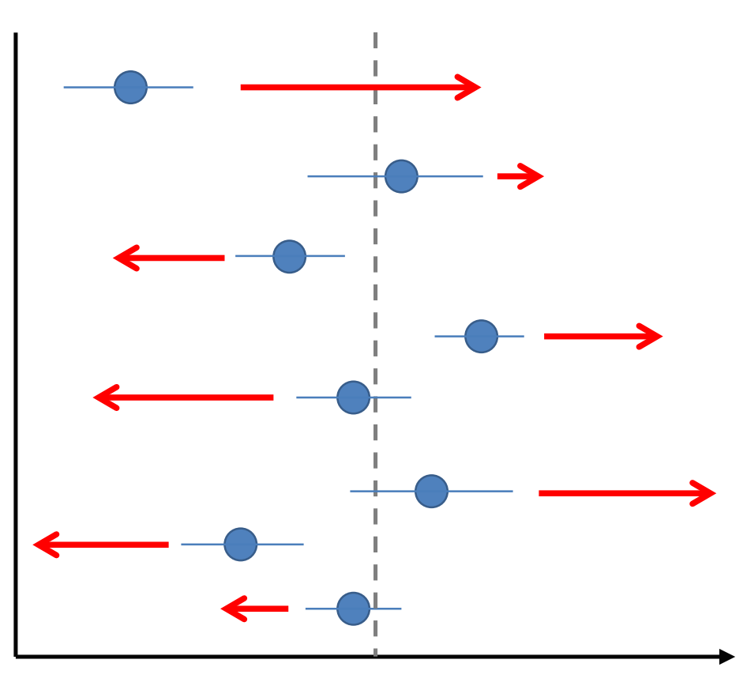
1. *Study group representation*
2. *Knowledge of group assignments*
3. *Exposure assessment methods lacking accuracy*
4. *Outcome assessment methods lacking accuracy*
5. *Potential confounding*
6. *Incomplete outcome data*
7. *Selective outcome reporting*
8. *Financial conflict of interest*
9. *Other*

Bias



vs.

Random Error



Exposure Assessment Criteria

- Evaluated each chemical separately by metric
- Criteria developed in collaboration with epidemiologists and air pollution experts
- Sample list of overall considerations for all metrics:
  - Quality of metric being used
  - Has metric been validated for scenario of use?
  - Was exposure a surrogate (i.e., distance to freeway)?
  - Did the analysis account for prediction uncertainty?
  - How was missing data accounted for?
  - Was sensitivity analysis performed?
- Sample list of specific considerations for modeling:
  - Type of model used
  - Quality of input data
  - Temporal specificity and variation
  - Whether meteorological variables were incorporated
  - Whether time-activity patterns were accounted for
- NOT used as checklist/scoring—used to guide reviewer's decisions on rating risk of bias for each data set
- Developed initial ratings for certain metric/chemicals where empirical information was available (Table 1)
- Discussion/consensus among reviewer authors to develop other initial ratings (i.e., TRI data, distance to freeway)
- Study-specific design considerations informed final ratings (Fig 1)
- Protocol with detailed risk of bias instructions was pre-published in PROSPERO


Welcome to PROSPERO
International prospective register of systematic reviews

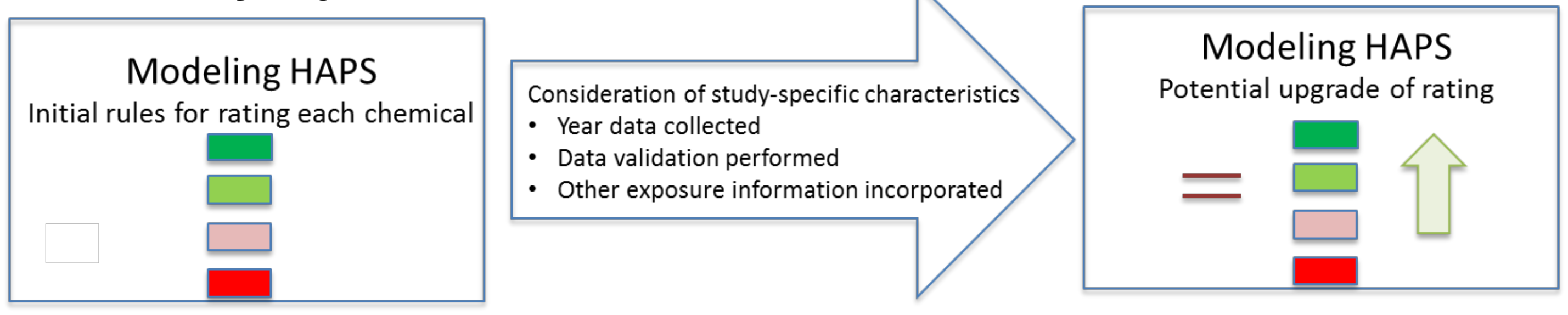
Results

- Screened 1,158 references and identified 23 human studies that met our inclusion criteria
- Studies varied widely in terms of methods, data source, and quantitative analysis of air pollution exposures
- Evaluated included studies separately for each chemical air pollution component by metric, leading to 194 study-metric-chemical ratings
- Risk of bias ratings ranged from "low" to "high"
- 7 studies available for PM$_{10}$—all used monitoring data. 6 studies were rated "probably low" and one study that used estimates from CALINE4 modeling rated "probably high" due to limitations in temporal accuracy of time to conception, and no person-level data available (Fig 2)
- 4 studies available for PM$_{2.5}$—three studies rated "probably low" with the same study above rated "probably high" for same reasons (Fig 2)
- Due to robustness and availability of data, PM data was incorporated into a meta-analysis
- 8 studies available for modeled mercury exposure—6 rated "high" from US EPA NATA or surrogate measure based on occupation and 2 rated "probably high" from US EPA TRI data (Fig 2)

Table 1. Initial HAPS ratings

HIGH Risk of Bias (ROB)		PROBABLY HIGH ROB		PROBABLY LOW ROB
Arsenic Beryllium Cadmium Mercury Nickel Chromium Hexachlorobenzene Manganese PCBs	Lead Acetaldehyde Acrolein Hydrazine Polycyclic Organic Matter Quinoline 7-PAH 1,3-Dichloropropene	Chloroform Diesel PM Ethylene Dibromide Ethylene Dichloride 1,1,2,2-Tetrachloroethane Formaldehyde	Perchloroethylene 1,3-Butadiene Coke Oven Emissions Propylene Dichloride Vinyl Chloride	Acrylonitrile Carbon Tetrachloride Ethylene Oxide Methylene Chloride Trichloroethylene Benzene

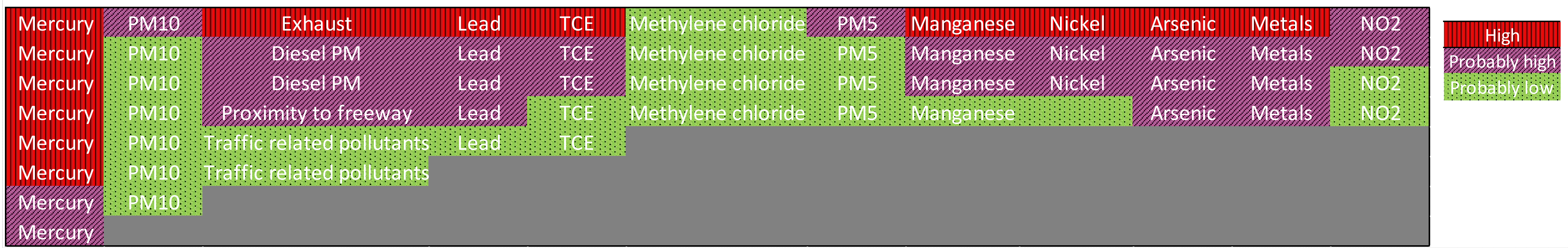
Figure 1. Initial HAPS ratings combined with study-specific considerations to reach final ratings


Modeling HAPS
Initial rules for rating each chemical

Consideration of study-specific characteristics
- Year data collected
- Data validation performed
- Other exposure information incorporated

Modeling HAPS
Potential upgrade of rating

Figure 2. Risk of bias results for chemicals with ≥4 ratings



Mercury	PM10	Exhaust	Lead	TCE	Methylene chloride	PM5	Manganese	Nickel	Arsenic	Metals	NO2
Mercury	PM10	Diesel PM	Lead	TCE	Methylene chloride	PM5	Manganese	Nickel	Arsenic	Metals	NO2
Mercury	PM10	Diesel PM	Lead	TCE	Methylene chloride	PM5	Manganese	Nickel	Arsenic	Metals	NO2
Mercury	PM10	Proximity to freeway	Lead	TCE	Methylene chloride	PM5	Manganese		Arsenic	Metals	NO2
Mercury	PM10	Traffic related pollutants	Lead	TCE							
Mercury	PM10	Traffic related pollutants									
Mercury	PM10										
Mercury											

Lessons Learned

- Challenges remain in evaluating validity of results from studies related to air pollution due to differences in quality of metrics used to measure exposure
- Exposure assessment tool was developed and tailored for this case study and study question of interest; modifications are likely needed for broader application
- Need for standard approaches to measure and report air pollution data in epidemiology studies
- Expert elicitation is time consuming and challenging, but is a necessity; systematic review process helps to make these judgments transparent and documented

Next Steps

- Currently applying this modified tool to a second proof of concept case study studying particulate matter air pollution and birth weight
- We have to date screened 540 references and identified 49 relevant studies
- We will apply the modified ROB tool to included studies, document the ratings, and evaluate the performance of the tool on this additional case study

Conclusions

- Accurate estimates of human exposure to air pollutants are necessary for evaluation of potential health risks and prioritization of interventions
- Evaluating risk of bias can help to identify threats to internal validity of air pollution exposure estimates in human observational studies
- We proposed and demonstrated the application of a tool that can be adapted and implemented for evaluating exposure assessment of future systematic reviews and can serve as a guide to strategically incorporate methods in the study design phase that reduce potential risk of bias in future air pollution studies

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