Review Panel on:

HEI Program to Assess Health Effects of Long-Term Exposure to Low Levels of Ambient Air Pollution

Final reports

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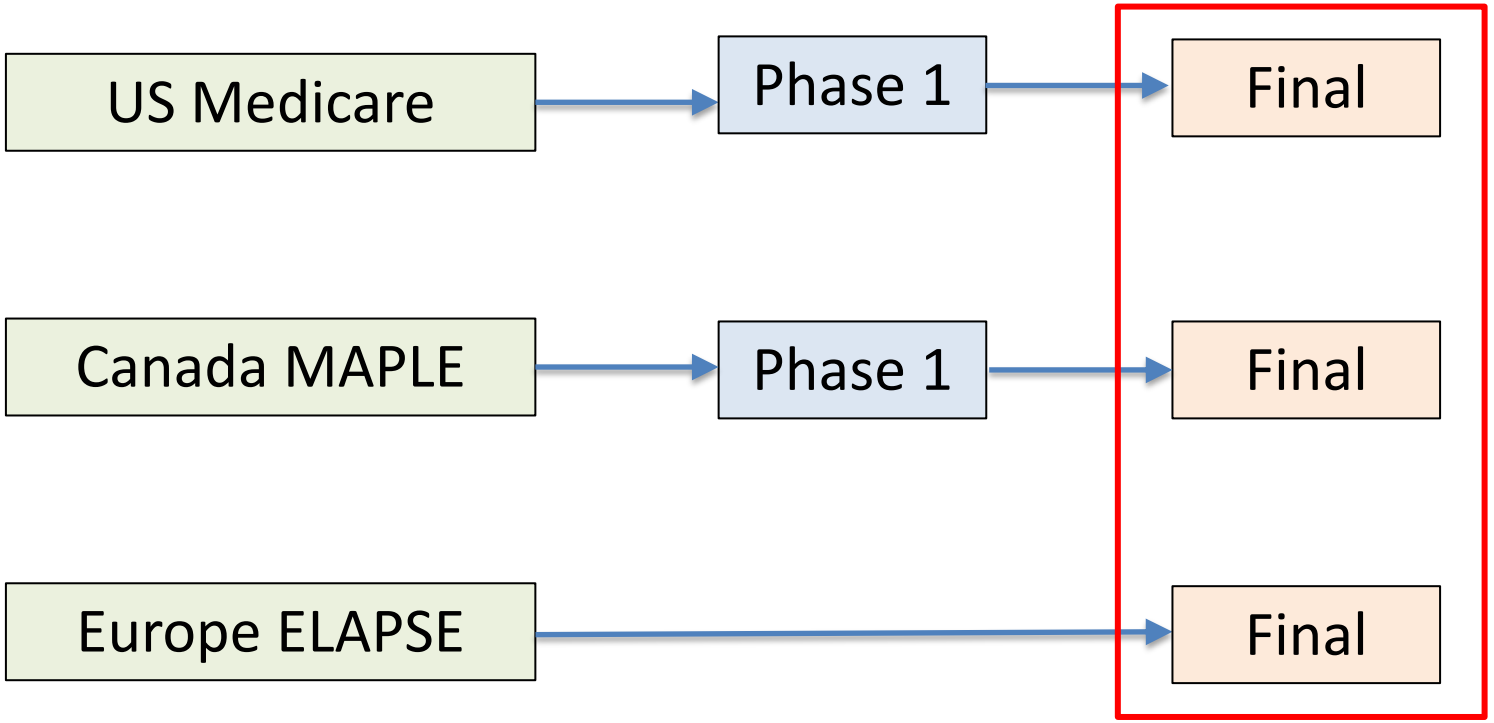
Some context for low levels

- plausibility – our Bayesian prior
- fewer susceptible to dying at low concentrations, so lots of data needed
- but, data quality inversely related to data quantity?
- advanced and new statistical methods
- causal modeling – revolution or another tool in the toolkit?

3 studies



Today's three overarching topics:

1. Multipollutant modeling and findings
2. Control of confounding, including "causal" modeling
3. Concentration-response functions (CRFs)

Multipollutant modeling and findings: MAPLE - Canada

- description –
  - 2 cohorts, 2nd for more confounder data
  - $PM_{2.5}$ (1x1km), O_3/Ox and NO_2 with different spatial resolution
- findings –
  - marked attenuation of $PM_{2.5}$ association & effect modification by Ox (not O_3)
- issues –
  - the matter of controlling for (and modification by) O_3 and Ox ("not a direct biological impact of the oxidant gases themselves")

Multipollutant modeling and findings: ELAPSE - Europe

- description –
  - ”pooled” (ESCAPE) and multiple administrative cohorts
  - $PM_{2.5}$, NO_2, O_3, BC all at 100x100m; only few “low”
- findings –
  - moderate attenuation of $PM_{2.5}$ association in “pooled” cohort, and more marked in administrative cohort
  - NO_2 assoc robust; O_3 assoc remains negative
- issues –
  - is attenuation due to confounding by co-pollutants?
  - the matter of negative association (& controlling) for O_3

Multipollutant modeling and findings: US Medicare

- description –
  - age ≥65 y
  - $PM_{2.5}$, NO_2, O_3 at 1×1 km, but applied to zip code
- findings –
  - $PM_{2.5}$ assoc robust to O_3, but attenuated when both O_3 and NO_2; NO_2 and O_3 assocs (positive here) largely unaffected with $PM_{2.5}$
- issues –
  - spatial scales
  - interpretation of attenuation

Control of confounding: MAPLE - Canada

- description –
  - control confounding with linear covariate terms in Cox models added stagewise
  - used smaller cohort allowing for indirect control of larger set of confounders
- findings – minimal impact of adjustment for added "behavioral" risk factors, but HRs vary by region
- issues –
  - indirect control of missing confounders
  - do marked differences in $PM_{2.5}$ effect by region in Canada indicate residual confounding or variation in toxicity?

Control of confounding: ELAPSE - Europe

- description –
  - linear terms in Cox models added in stages
  - ancillary survey data for additional confounders, allowing indirect adjustment in Cox model
- findings –
  - $PM_{2.5}$ and NO_2 (not O_3) effects increase in 4/7 admin cohorts (incl Norway) with more confounders
  - impacts inconsistent when adding external confounders
- issues –
  - indirect control (Shin method) of missing confounders

Control of confounding, including "causal" modeling: US Medicare

- description –
  - also use ancillary data set for additional confounders
  - "causal" modeling only here, so far
- findings –
  - $PM_{2.5}$ effects insensitive to traditional addition of added confounders
  - "causal" modeling results largely consistent with traditional modeling, although attenuated at low conc
- issues –
  - advantages/assumptions of "causal" models
  - other approach for unmeasured confounders

Concentration-response functions: MAPLE - Canada

- description –
  - has the lowest $PM_{2.5}$ concentrations
  - used cubic (and restricted) smoothing spline
  - SCHIF (Shape-Constrained Health Impact Function) originally only here, then eSCHIF
  - also analyses restricted to low concentrations
- findings –
  - supralinear with flattening at higher concentrations

Concentration-response functions: MAPLE - Canada

- issues –
  - wiggly CRFs using smoothing splines – because of large data sets?
  - what about the SCHIF? CIs narrowest at minimum concentrations
  - understanding flattening at higher concentrations

Concentration-response functions: ELAPSE - Europe

- description –
  - used natural smoothing spline
  - also applied SCHIF
  - and analyses restricted to low concentrations
- findings –
  - also supralinear with flattening at higher concentrations
- issues
  - understanding flattening at higher concentrations
  - different countries/populations contributing to different parts of CRF

Concentration-response functions: US Medicare

- description –
  - used kernel smoother
  - and analyses restricted to low concentrations
- findings –
  - largely linear CRFs, although HRs larger at $PM_{2.5}$<12 ug/m^3
- issues –
  - characterizing CRF as ”linear” doesn’t reflect the apparent larger $PM_{2.5}$ HRs at low (<12ug/m^3) concentrations

In summary: multipollutant modeling and findings

- some evidence for “confounding” by co-pollutants, but issues raised about multi-pollutant models are still largely unresolved
- different spatial scales of pollutant predictions and of ambient concentrations are problematic
- the uncertain matter of ozone

In summary: control of confounding, including ”causal” modeling

- associations generally persist with more confounder control, although some evidence for impact of better control
- assess success of application of “indirect” methods for enhancing control of confounders
- want to conclude “causal” based on observational data; how to weight findings from ”causal” modeling?
- unmeasured confounders?

In summary: concentration-response functions (CRFs)

- approaches to addressing low concentration issue
  - 1) restriction; 2) modeling the CRF; 3) threshold models
- low concentration associations in all cohorts
- largely supralinear/linear shapes
  - "most potential for harm at low levels" - difficult to swallow, but:
    - example: diff between 5ug/m^3 and 15, vs 40 and 50
    - toxicology: dose-dependent transitions
  - the SCHIF
- threshold models no better fit than non-threshold models

Next Steps for the Review Panel

1. completion of the commentaries
2. integrative synthesis of all three studies

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