

Concentration Response Functions in ELAPSE, Medicare, and MAPLE cohorts

ELAPSE



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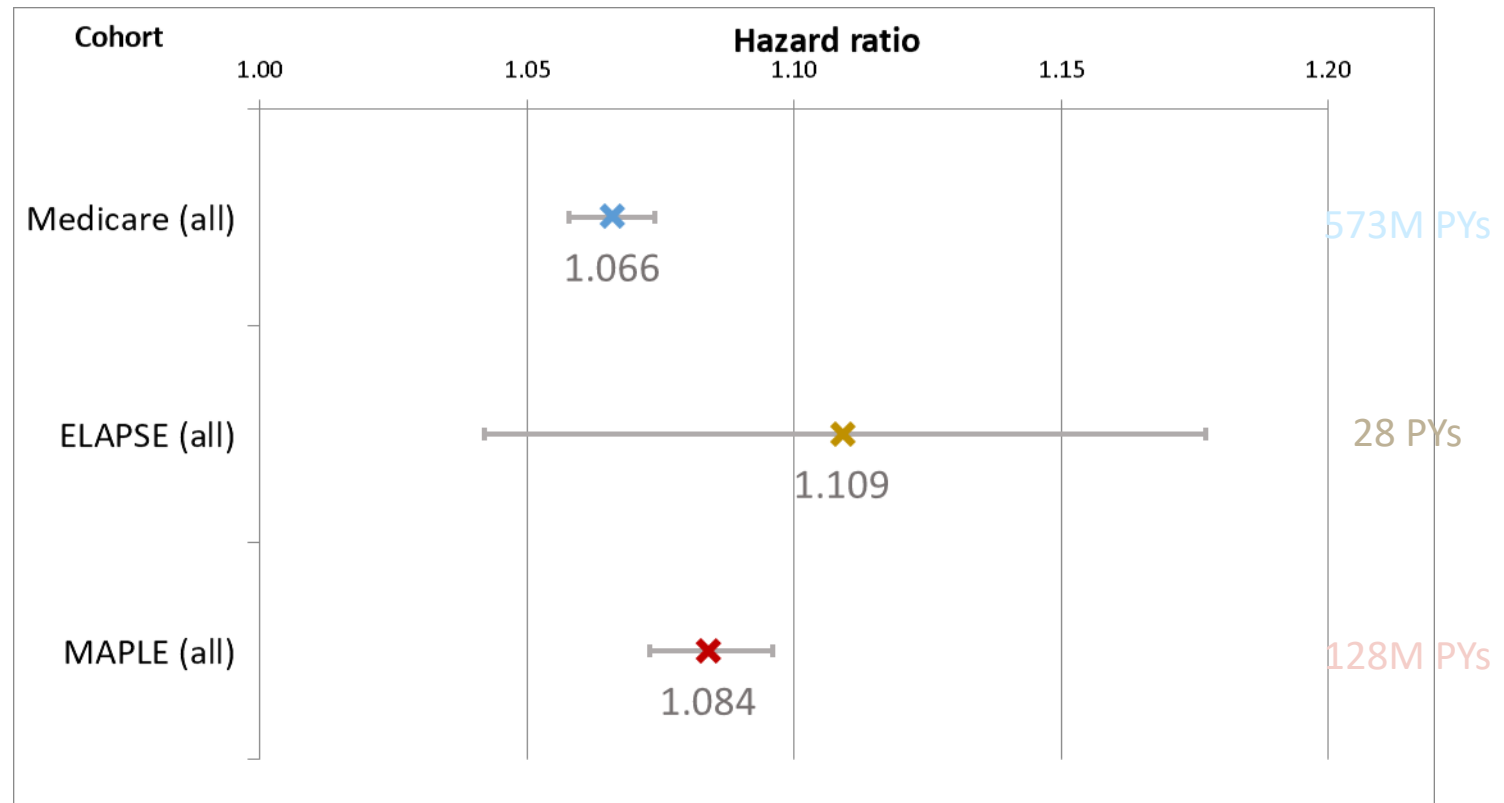
TANYA CHRISTIDIS ON BEHALF OF THE MAPLE, ELAPSE, AND HARVARD(MEDICARE) TEAMS

What do the linear models tell us

6 to 11% increased risk of mortality

Highest risk in Europe; Canada and the United States lower

Cox proportional hazard ratios of mortality* per increase of $10\mu\text{g}/\text{m}^3$ of $\text{PM}_{2.5}$



Medicare: all-cause mortality; ELAPSE: natural cause mortality; MAPLE: non-accidental mortality

Linear model limitations

Assumes the same relationship between $PM_{2.5}$ and mortality at all levels of $PM_{2.5}$

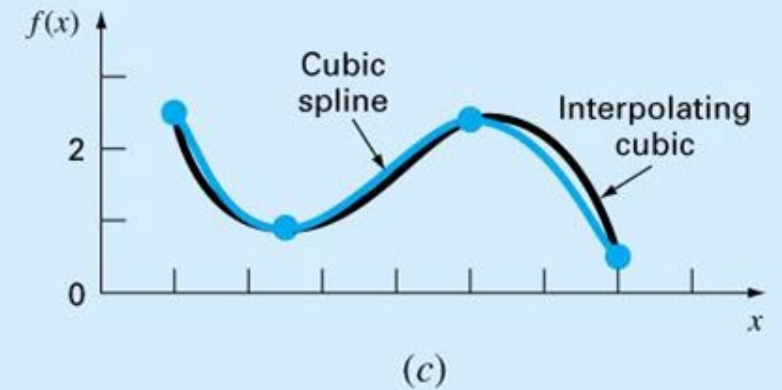
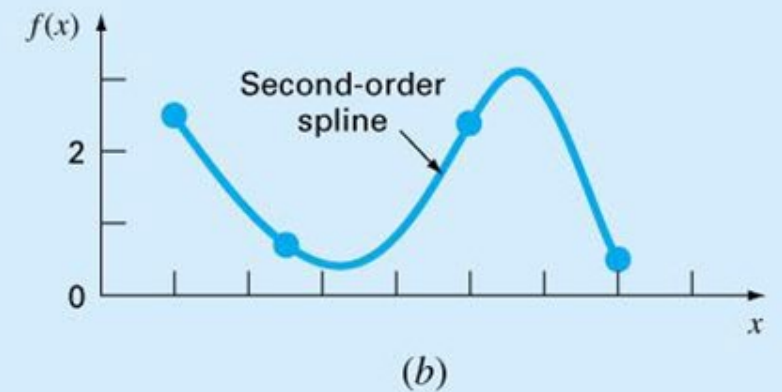
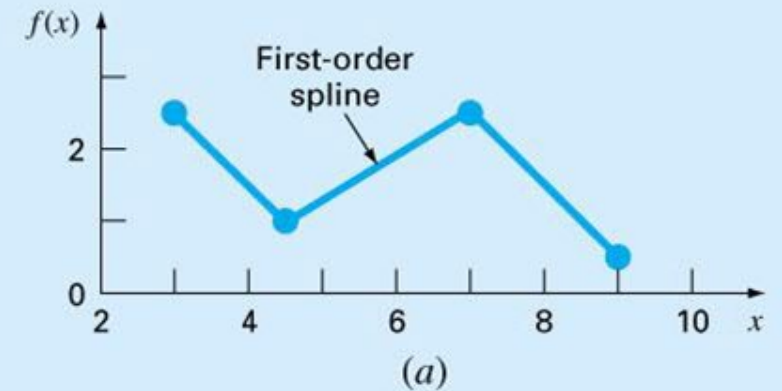
Confounders impact the relationship between PM and mortality uniformly at all levels of $PM_{2.5}$

No insight into threshold

Cubic Splines

Spline: Establish some points (knots) and then connect them (which predicts the values between knots)

Spline allows for a different relationship between $PM_{2.5}$ and mortality at different levels of $PM_{2.5}$

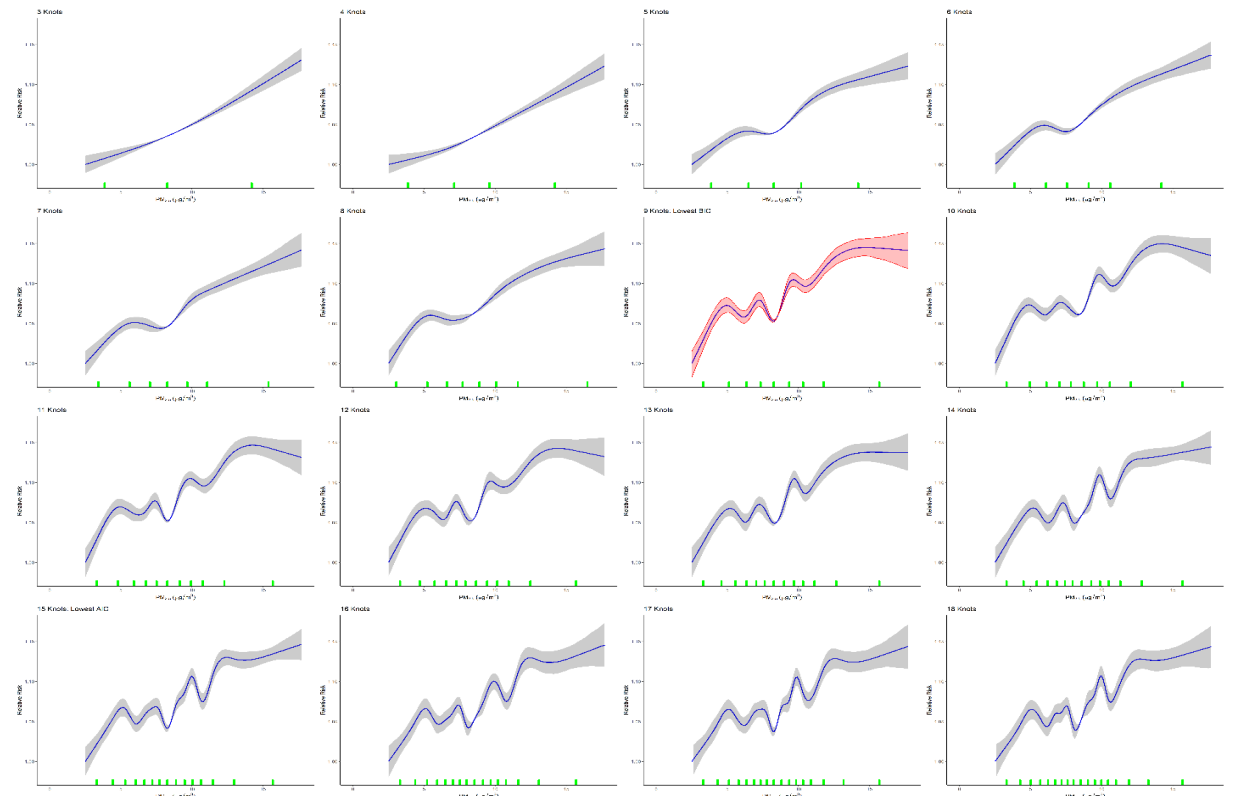


Cubic Spline Limitations

The challenge is to find a curve that:

- best represents the data (i.e., flexible)
- is useful for risk assessment (i.e., not too wiggly)

MAPLE restricted cubic spline predictions, from 3 to 18 knots



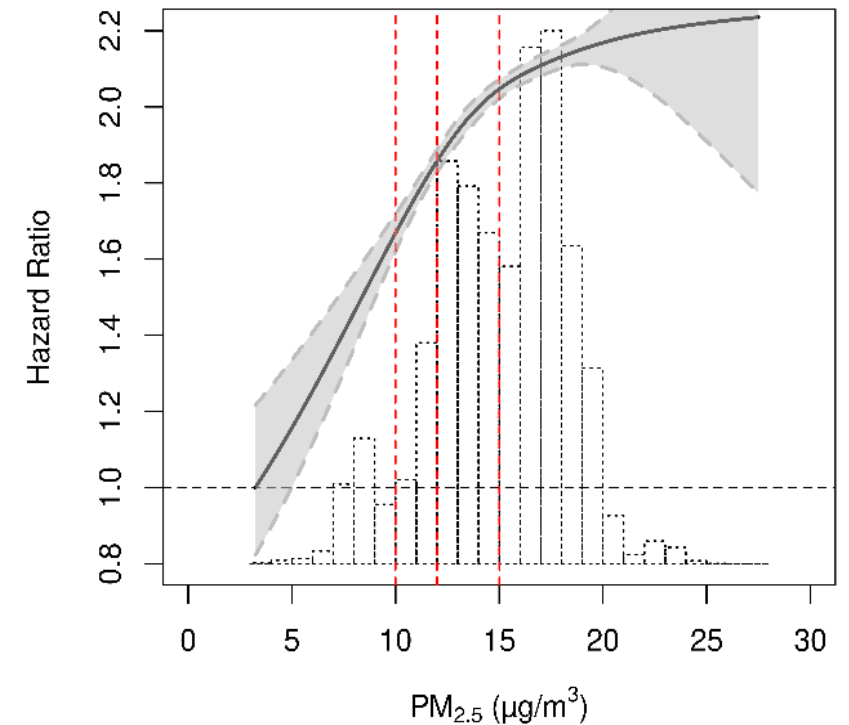
ELAPSE uses a Natural Spline

a priori selection

Findings:

- Linear below the lowest and above the highest knot concentration
- No wiggles
- No low level threshold in mean predictions
- Flattening of curve at higher concentrations

ELAPSE natural spline, natural cause mortality, two knots



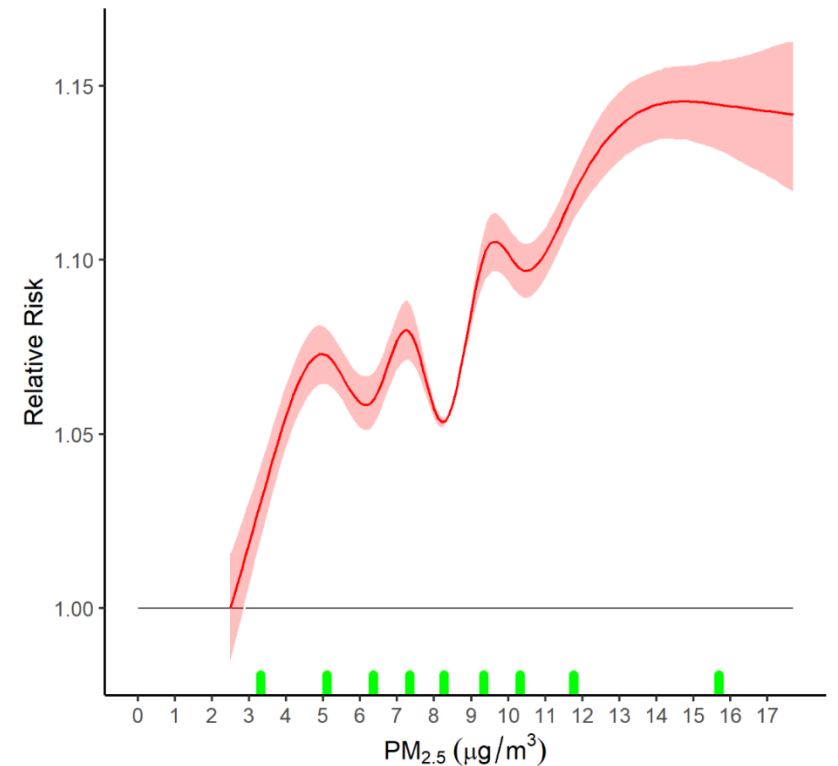
MAPLE Uses a Restricted Cubic Spline

Controlled search for best fit

Findings:

- The best fitting spline (9 knots) wiggly between 5 and 12 $\mu\text{g}/\text{m}^3$
- Lower CI above 1 starting at 2.9 $\mu\text{g}/\text{m}^3$, close to minimum of 2.5 $\mu\text{g}/\text{m}^3$

MAPLE restricted cubic spline, non-accidental mortality, 9 knots





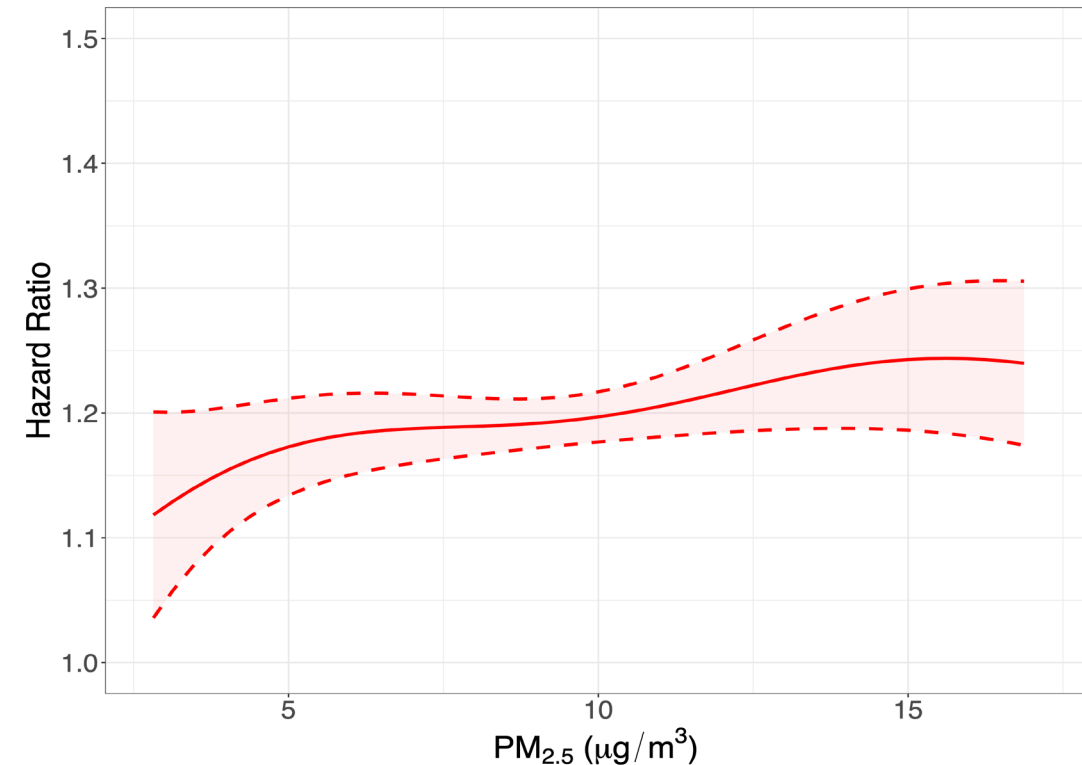
Medicare uses Kernel smoothing

Fit within causal inference framework

Findings:

- Gradual changes in curvature (increase at low concentrations, then flattens, then increases, then flattens again)
- Almost linear at levels lower than current standards
- Controlled curvature with smoothing parameters

MEDICARE causal exposure-response curve, all-cause mortality, kernel for every obs.



Controlling the Amount of Curvature

Want a curve that is meaningful for risk assessment

ELAPSE Used Shape-Constrained Health Impact Function (SCHIF)

- Plausible **sigmoidal** shapes
- Curvature controlled by limiting parameters
- Model is a weighted average of all shapes examined

ELAPSE SCHIF

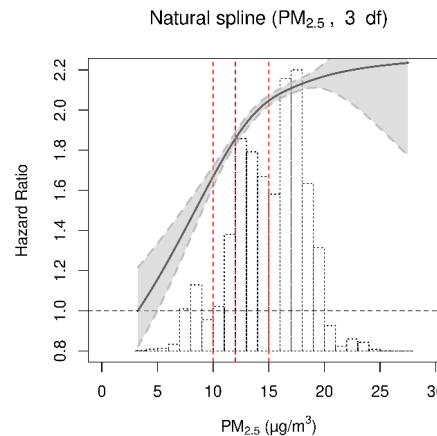
Findings:

- Low uncertainty at minimum
- Supralinear trend
- Lower CI above 1 at 5 $\mu\text{g}/\text{m}^3$

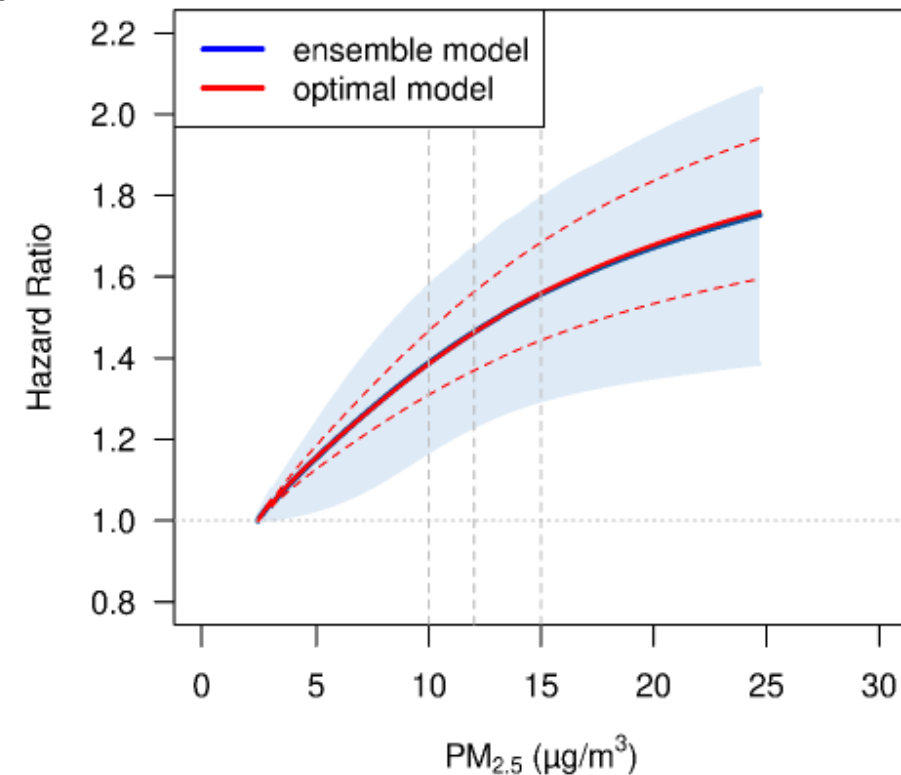
SCHIF limitations:

- Each SCHIF fit to entirety of data
- No local fitting where data are sparse
- May not cover all possible shapes of interest

ELAPSE natural spline, natural cause mortality, two knots



ELAPSE SCHIF, natural cause mortality



eSCHIF: adapting SCHIF to Spline fits

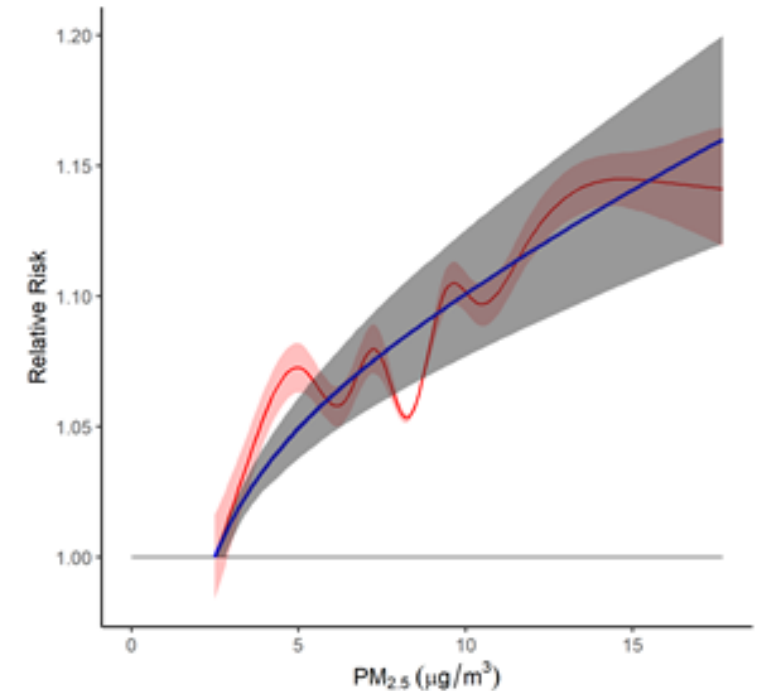
Extended SCHIF (eSCHIF) fit SCHIF algebraic formula to **spline** predictions

eSCHIF maintains uncertainty characterisation at low concentrations

Supralinear

SCHIF/eSCHIF can be directly implemented in air quality assessment research and benefits analysis

MAPLE eSCHIF and restricted cubic spline, non-accidental mortality



Associations at select concentrations

What is the lowest concentration at which we have evidence of a relationship between PM_{2.5} and mortality?

Retain persons or person-years with exposures below a specific level

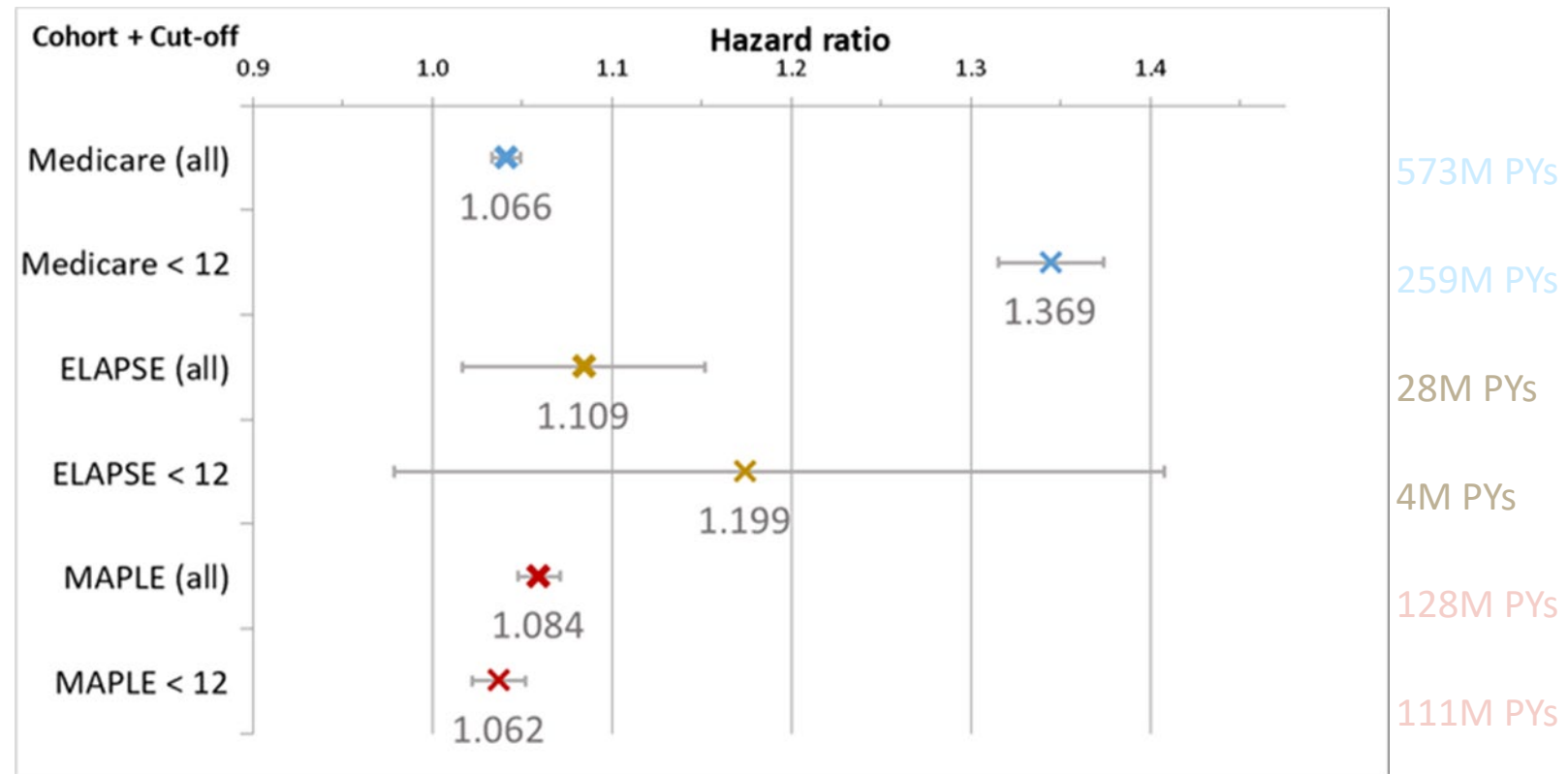
- ELAPSE restricted to under 25, 20, 15, 12, and 10 $\mu\text{g}/\text{m}^3$
- Medicare and MAPLE restricted to under 12 $\mu\text{g}/\text{m}^3$

Associations under $12 \mu\text{g}/\text{m}^3$

Risk remains even for those who have only low level exposure

Higher uncertainty in these sub-populations

Cox proportional hazard ratios of mortality* per increase of $10\mu\text{g}/\text{m}^3$ of $\text{PM}_{2.5}$



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Standard Threshold Model

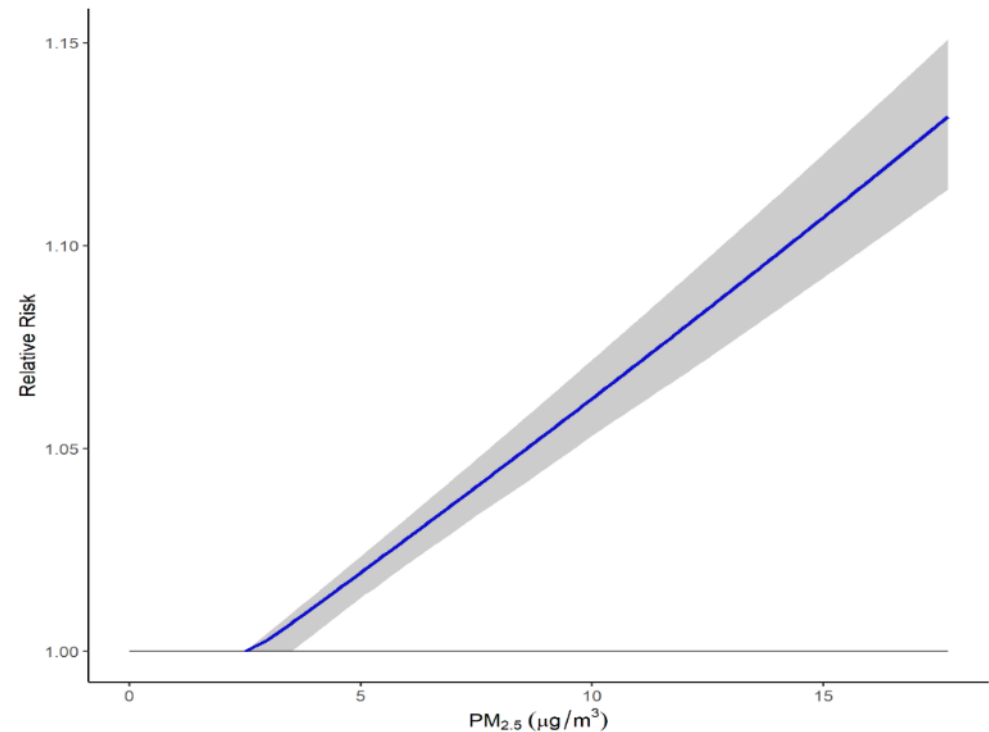
Standard threshold model with thresholds at 2.5-10 $\mu\text{g}/\text{m}^3$ by increments of 0.5

Ensemble weighting

Strong evidence of positive associations at low concentrations

Lower CI > 1 at 3.5 $\mu\text{g}/\text{m}^3$

MAPLE Classic Threshold Model, Non-Accidental Mortality



Conclusions

Evidence for PM_{2.5} -mortality association at low levels in all studies

MAPLE and ELAPSE curves were supralinear

- Steepest slope at lowest levels and plateau at high levels
- With increasing concentrations the marginal changes in risk appear to decline

Medicare curve was near-linear

- Indicates aggravated effects at all levels PM_{2.5}

Positive association between PM_{2.5} and mortality observed even at the lowest levels

Ongoing CRF work

Each team will use the eSCHIF method in the harmonized analysis

- Administrative cohorts only
- Limiting to age 65+
- Covariate inclusion will be harmonized
- Each team will use MAPLE PM_{2.5} (v2m) 1km x 1km, from 2001 to 2016
- Examining all cause mortality

ELAPSE



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Thanks!

Extra slides if time allows

Low concentration shape and uncertainty

As # of knots and improvement of fit increases, so too does wiggleness

Low concentration shape and uncertainty stable for # knots > 4

