Determinants of the magnitude and shape of the associations between long-term $PM_{2.5}$ exposure and mortality: harmonized analyses in three large cohort studies in Canada, United States and Europe

HEI Annual Conference

June 27, 2022

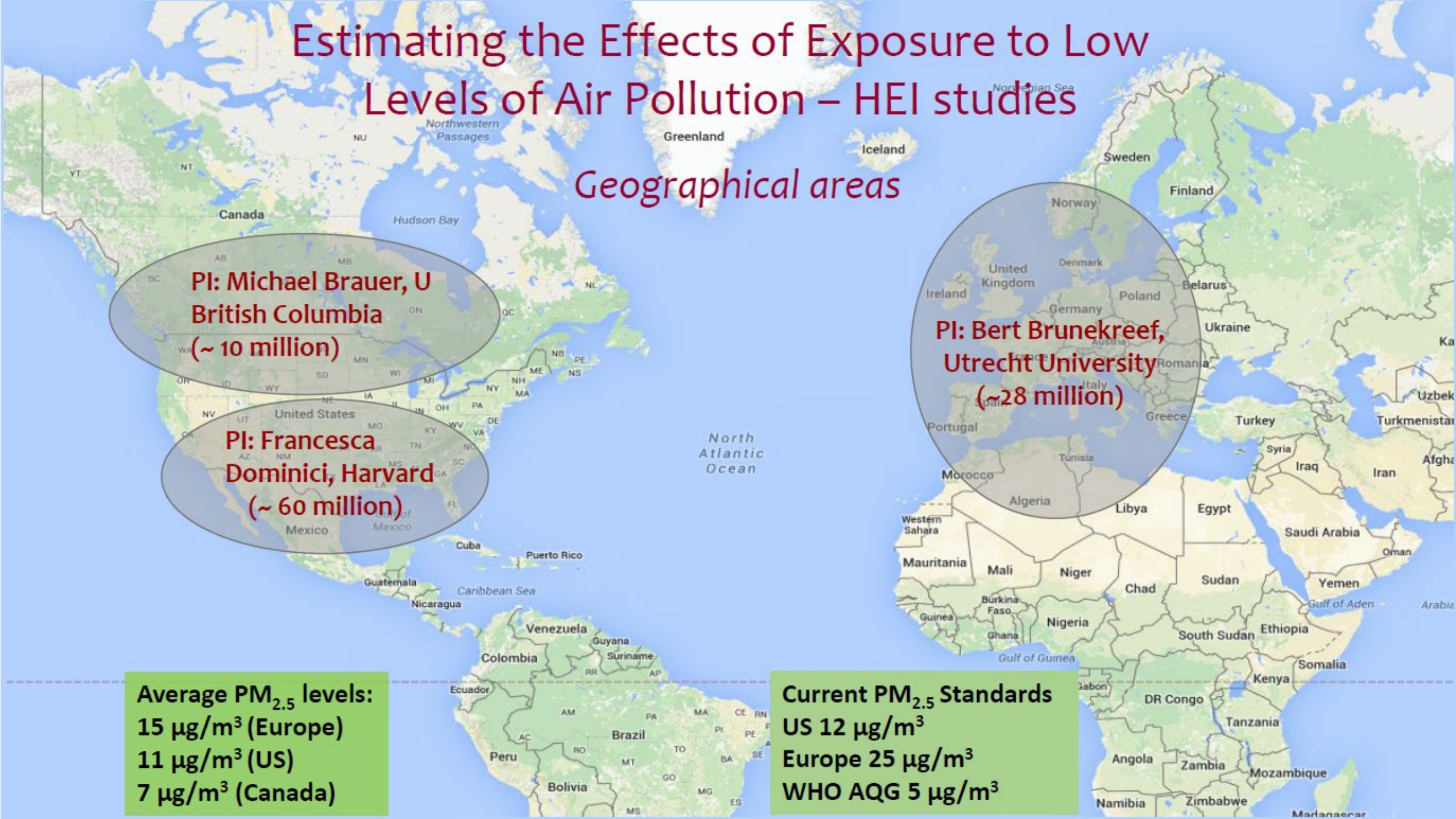
Jie Chen on behalf of the ELAPSE, MAPLE and Harvard teams

Background

- A **causal** relationship between long-term fine PM ($PM_{2.5}$) exposure and all-cause mortality (2019 ISA, US EPA), indicating population health benefits of reductions in $PM_{2.5}$ concentrations;
- Evaluating the benefits of reductions in concentrations depends upon understanding both the **magnitude** of the $PM_{2.5}$ mortality risk and the **shape** of this relationship;
- Positive associations generally reported with varying magnitude across studies
- Heterogeneity related to study population, level of $PM_{2.5}$ exposure, composition $PM_{2.5}$ mixture, exposure assessment, statistical models...
- Little systematic evaluation of these factors

Estimating the Effects of Exposure to Low Levels of Air Pollution – HEI studies

Geographical areas



Average $PM_{2.5}$ levels:
15 µg/m³ (Europe)
11 µg/m³ (US)
7 µg/m³ (Canada)

Current $PM_{2.5}$ Standards
US 12 µg/m³
Europe 25 µg/m³
WHO AQG 5 µg/m³

RESEARCH REPORT

HEALTH EFFECTS INSTITUTE

Number 208
September 2021

Mortality and Morbidity Effects of Long-Term Exposure to Low-Level $PM_{2.5}$, BC, NO_2, and O_3: An Analysis of European Cohorts in the ELAPSE Project

Bert Brunekreef, Maciej Strak, Jie Chen, Zorana J. Andersen, Richard Atkinson, Mariska Bauwelinck, Tom Bellander, Marie-Christine Boutron, Jørgen Brandt, Iain Carey, Giulia Cesaroni, Francesco Forastiere, Daniela Fecht, John Gulliver, Ole Hertel, Barbara Hoffmann, Kees de Hoogh, Danny Houthuijs, Ulla Hvidtfeldt, Nicole Janssen, Jeanette Jørgensen, Klea Katsouyanni, Matthias Ketzel, Jochem Klompmaker, Norun Hjertager Krog, Shuo Liu, Petter Ljungman, Amar Mehta, Gabriele Nagel, Bente Oftedal, Göran Pershagen, Annette Peters, Ole Raaschou-Nielsen, Matteo Renzi, Sophia Rodopoulou, Evi Samoli, Per Schwarze, Torben Sigsgaard, Massimo Stafoggia, Danielle Vienneau, Gudrun Weinmayr, Kathrin Wolf, and Gerard Hoek

RESEARCH REPORT

HEALTH EFFECTS INSTITUTE

Number 211
January 2022

Assessing Adverse Health Effects of Long-Term Exposure to Low Levels of Ambient Air Pollution: Implementation of Causal Inference Methods

Francesca Dominici, Antonella Zanobetti, Joel Schwartz, Danielle Braun, Ben Sabath, and Xiao Wu

RESEARCH REPORT

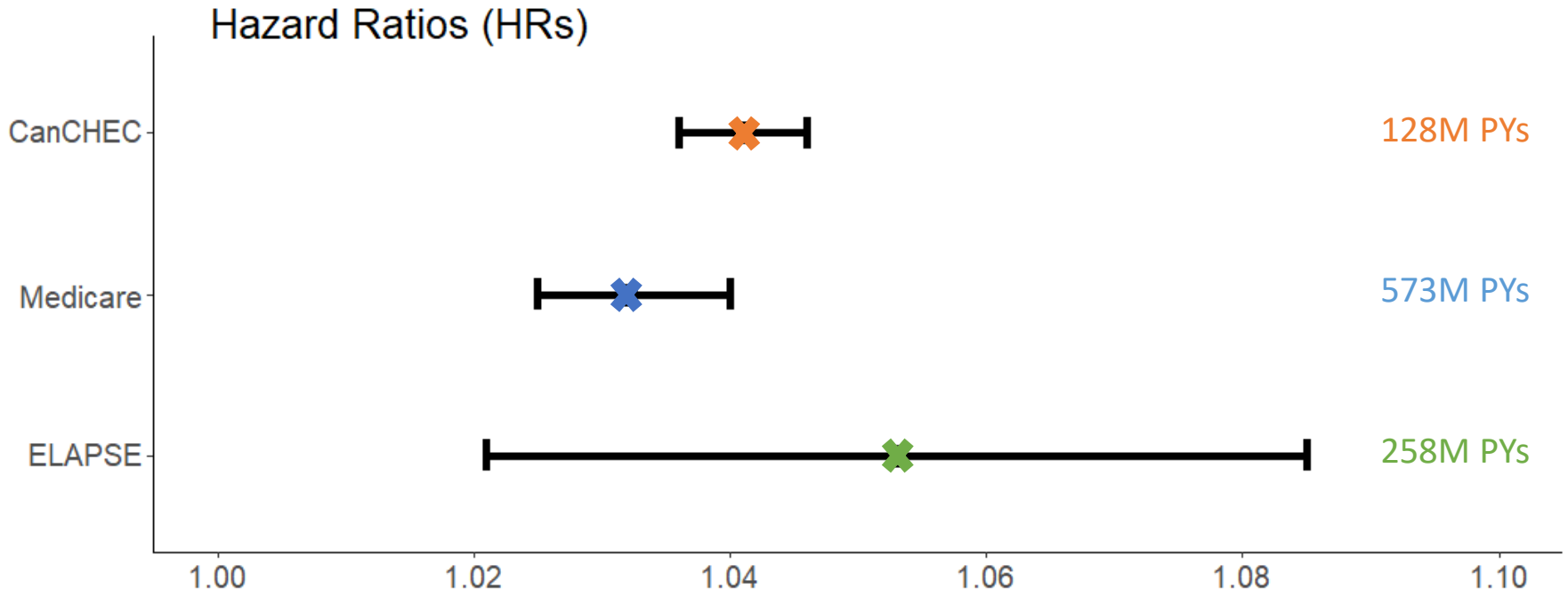
HEALTH EFFECTS INSTITUTE

Number 203
November 2019

Mortality–Air Pollution Associations in Low-Exposure Environments (MAPLE): Phase 1

Michael Brauer, Jeffrey R. Brook, Tanya Christidis, Yen Chu, Dan L. Crouse, Anders Erickson, Perry Hystad, Chi Li, Randall V. Martin, Jun Meng, Amanda J. Pappin, Lauren L. Pinault, Michael Tjepkema, Aaron van Donkelaar, Scott Weichenthal, and Richard T. Burnett

Cox proportional hazard ratios of mortality per 5µg/m^3 increase of $PM_{2.5}$



	Study populations	Exposure	Outcome	Covariates	…
MAPLE	"stacked" 1991, 1996, 2001 CanCHEC **ages > 25 yrs**	1×1 km	**Natural** mortality		
Medicare	Medicare enrollees from 2000 to 2016 **ages ≥ 65 yrs**	1×1 km	**All-cause** mortality	Limited available at individual level	
ELAPSE	Seven administrative cohort participants **ages ≥ 30 yrs**	100×100 m	**Natural** mortality		

Aim

- To investigate and discuss the impact of determinants on the associations between long-term $PM_{2.5}$ exposure and mortality, by performing harmonized analyses across three large studies in Canada (MAPLE), the United States (Medicare) and Europe (ELAPSE).

Methods: harmonized analysis

	Study populations	Exposure	Outcome	Covariates	…
MAPLE	"stacked" 1991, 1996, 2001 CanCHEC **ages > 25 yrs**	1×1 km	**Natural** mortality		
Medicare	Medicare enrollees from 2000 to 2016 **ages ≥ 65 yrs**	1×1 km	**All-cause** mortality	Limited available at individual level	
ELAPSE	Seven administrative cohort participants **ages ≥ 30 yrs**	100×100 m	**Natural** mortality		
Harmonized	Participants **ages ≥ 65 yrs**	1×1 km MAPLE method	**All-cause** mortality	Common covariate models	

- **Statistical analysis:**

➢ **Linear association** – Cox proportional hazard models incorporating $PM_{2.5}$ as time-varying exposure. **Common covariate models specified** (next page)

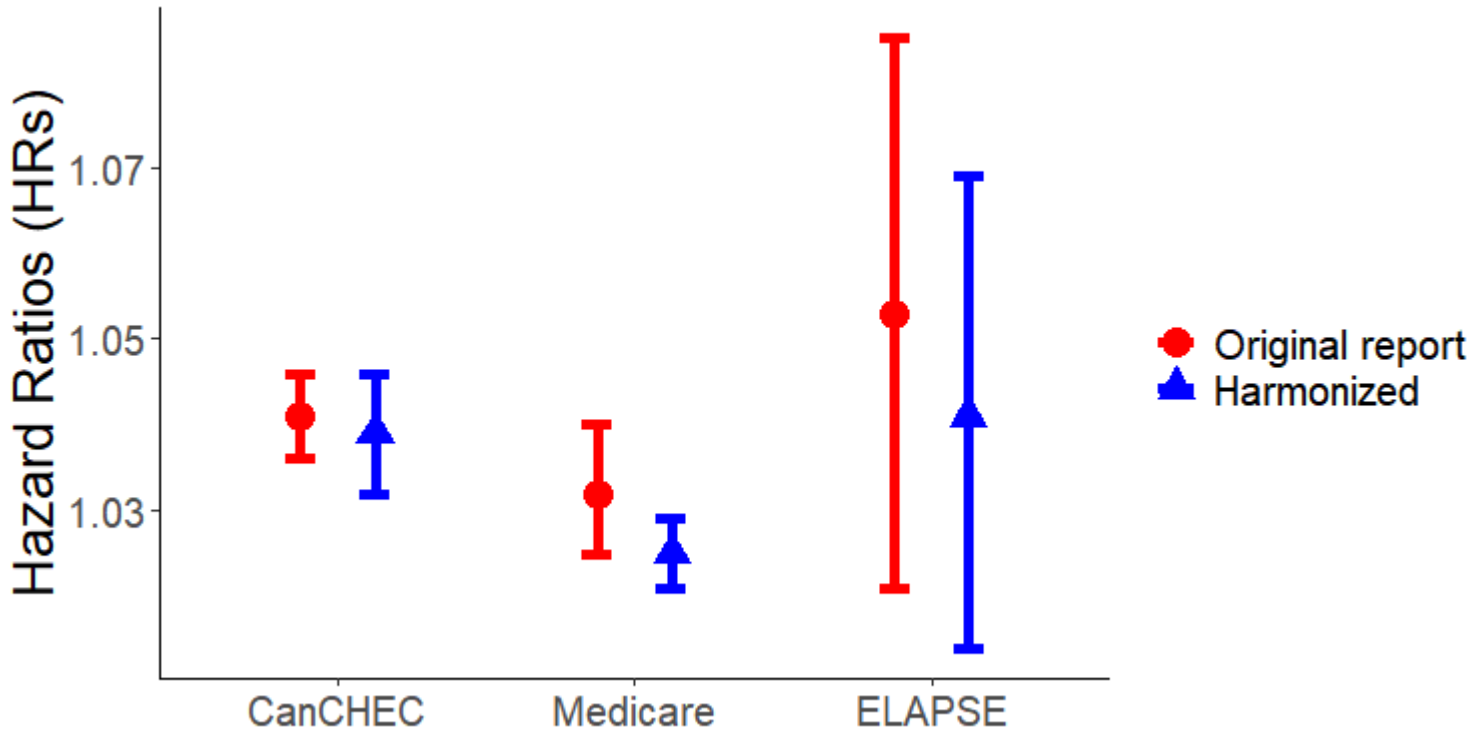
➢ **Exposure-response relationships – extended Shape-Constrained Health Impact Function** (eSCHIF), which relates risk to concentration suitable for quantitative benefits analysis.

Methods: Common covariate models with increasing control of potential confounders

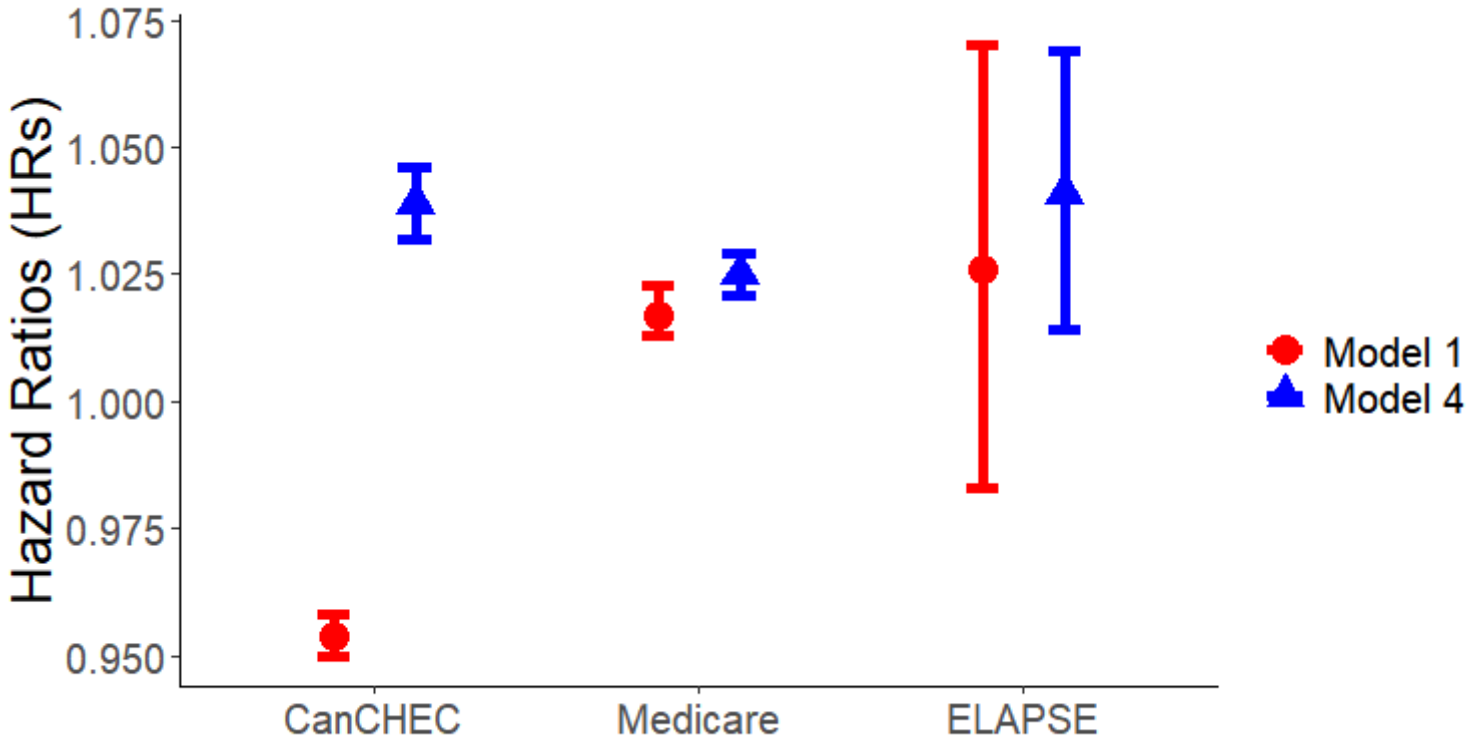
	Stacked CanCHEC	Medicare	Belgian	Danish	Dutch	Norwegian	Roman	Swiss
Model 1								
Individual-level covariates								
Age	×	×	×	×	×	×	×	×
Sex	×	×	×	×	×	×	×	×
Follow-up year	×	×	×	×	×	×	×	×
Model 2								
Variable representing Race/Ethnicity	Immigrant status, visible minority status, indigenous identity	Race/Ethnicity	Country origin	Country origin	Country origin	-	-	Country origin
Variable representing SES	Income	Medicaid eligibility	Education	Income	Income	Income	Education	Education
Area-level covariates								
Model 3								
Composite SES index	×	-	-	-	×	-	×	×
(Household) income	-	×	×	×	×	×	×	-
Median house value	-	×	-	-	-	-	-	-
Residents in poverty (%)	-	×	-	-	-	-	-	-
Residents that own their house (%)	-	×	-	-	-	-	-	-
Education	-	×	×	×	-	×	×	×
Unemployment rate	-	-	×	×	×	×	×	×
Non-western ethnic rate	-	-	×	-	×	-	-	-
Model 4								
No. of regional indicators	6	4	3	5	12	7	NA	7

RESULTS

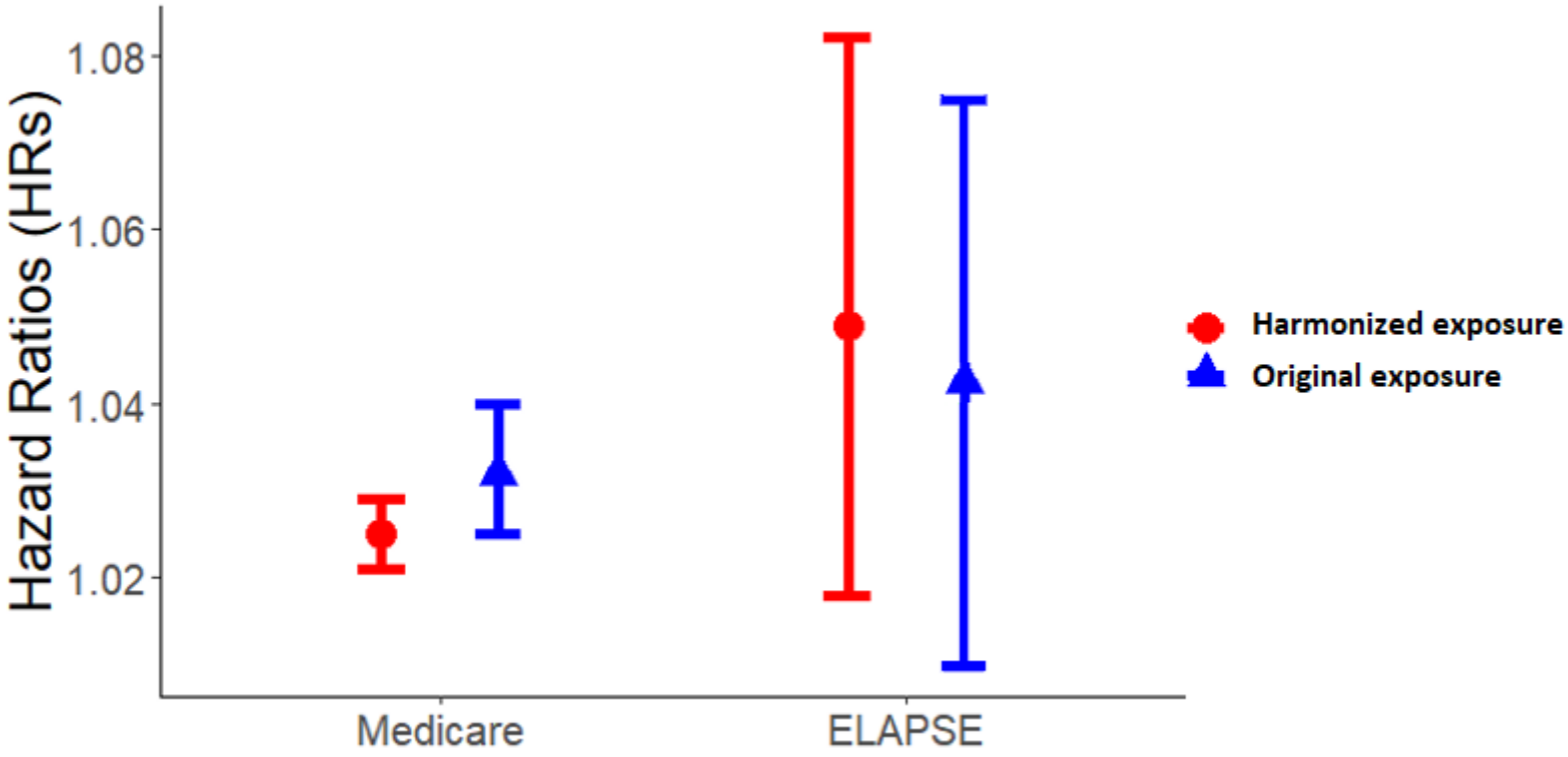
HRs for $PM_{2.5}$ per 5 µg/m^3 from Harmonized Model 4 and Original studies



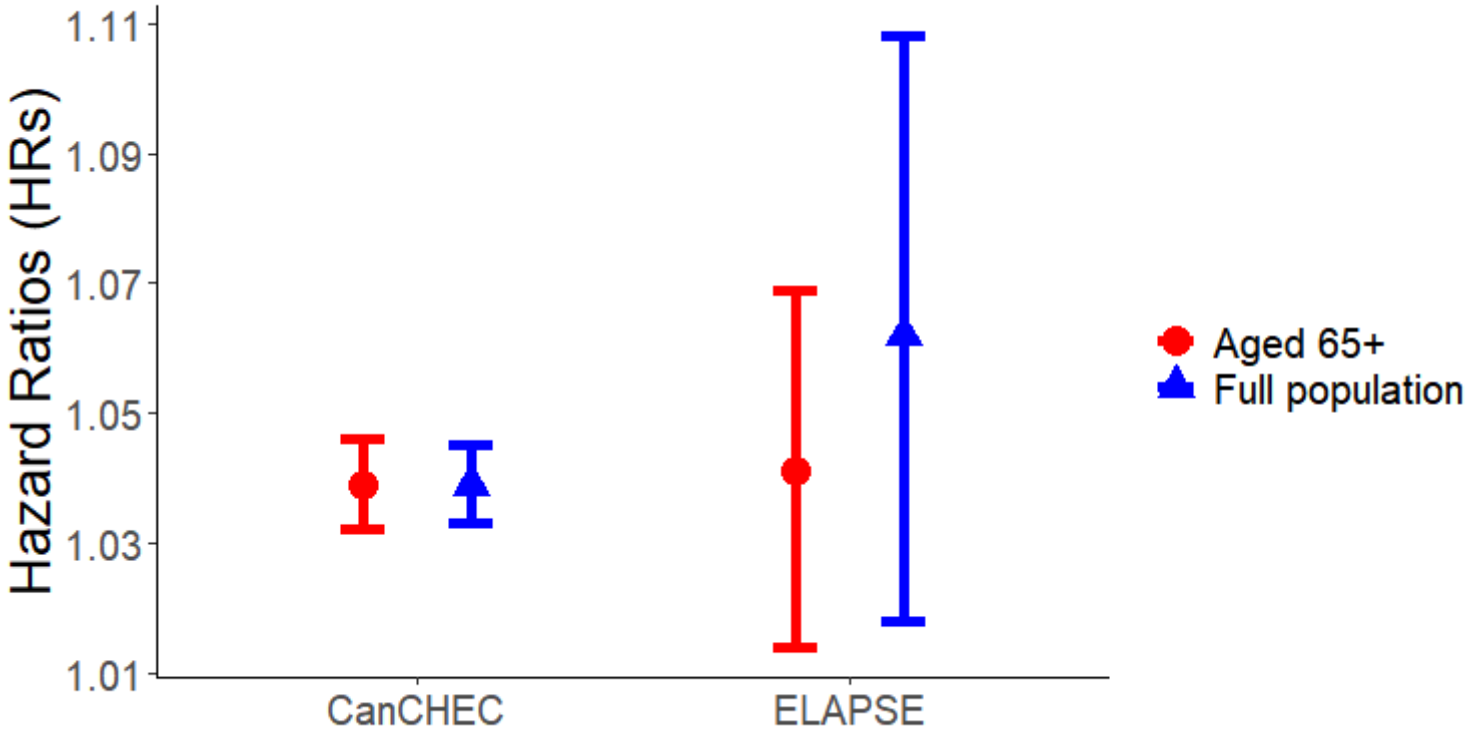
HRs for $PM_{2.5}$ per 5 µg/m^3 from Model 1 (minimally adjusted model) and Model 4 (main model)



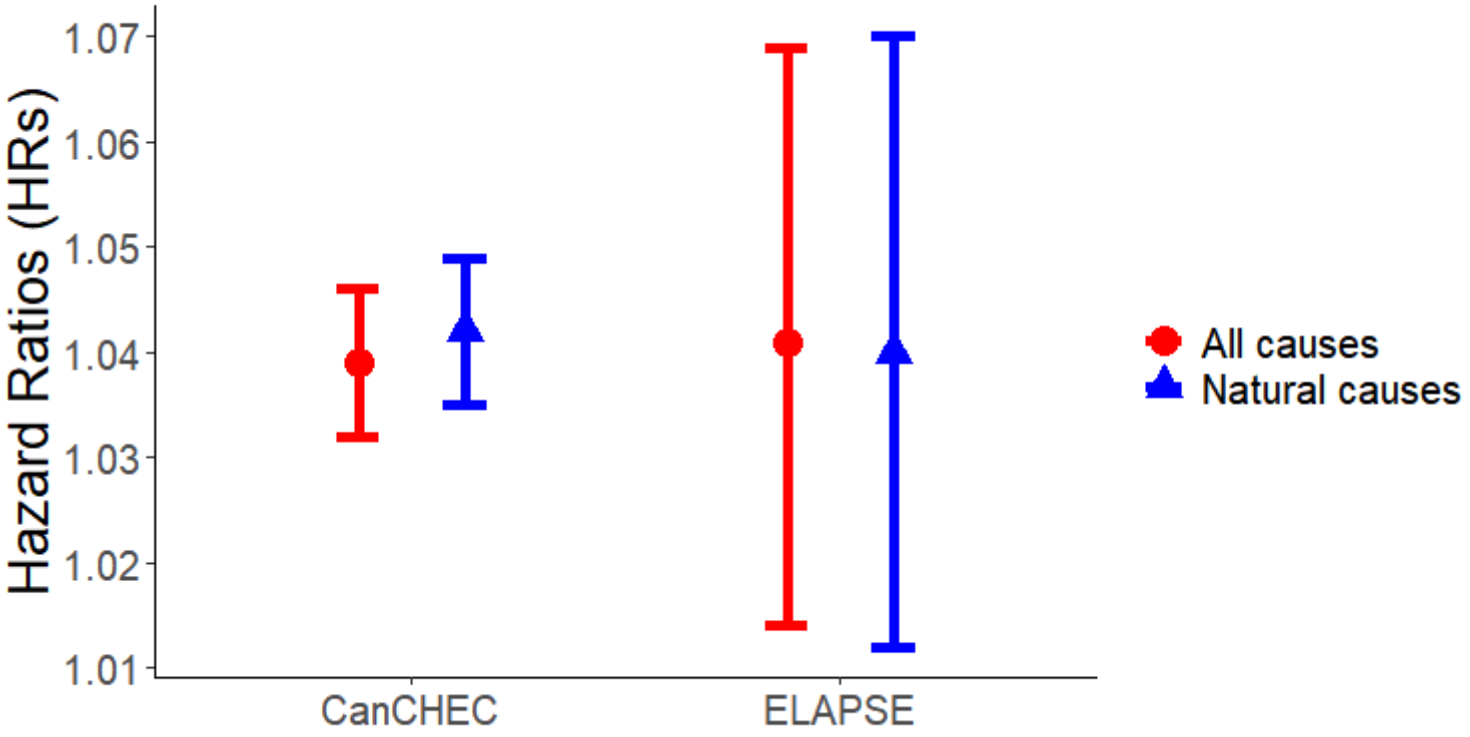
HRs for $PM_{2.5}$ per 5 $\mu g/m^3$ from harmonized exposure assessment and the original exposures applied in Medicare and ELAPSE



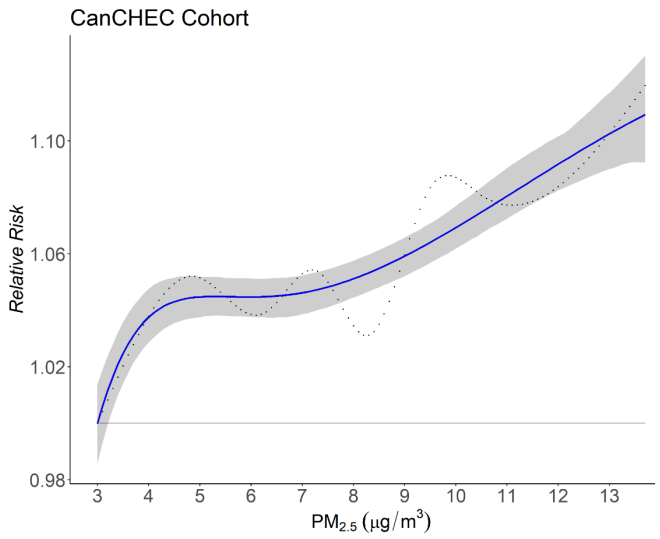
HRs for $PM_{2.5}$ per 5 µg/m^3 in study populations aged 65+ and full populations in CanCHEC (aged 25+) and ELAPSE (aged 30+)

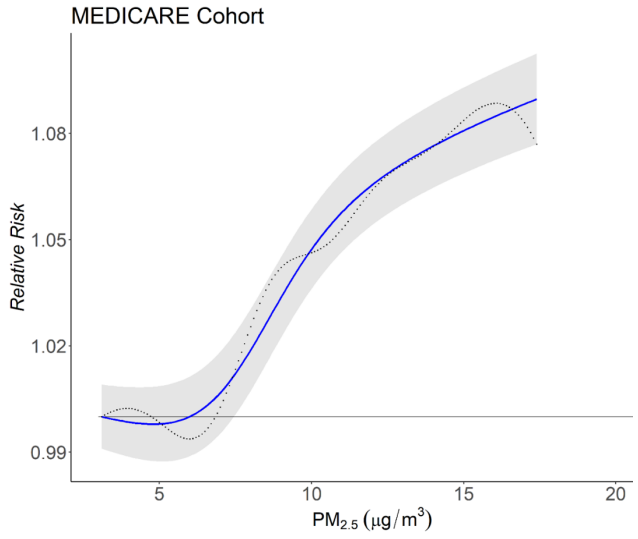


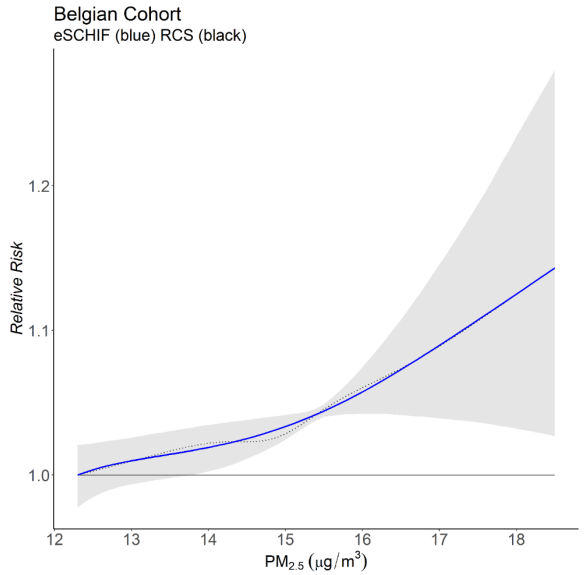
HRs for $PM_{2.5}$ per 5 µg/m^3 for mortality from all causes and natural causes

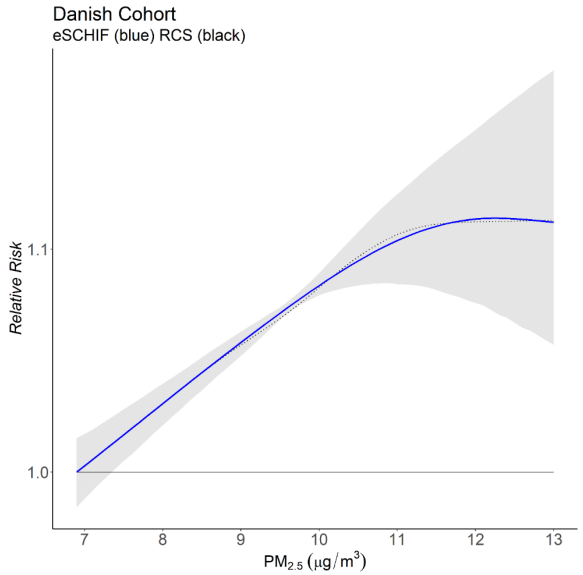


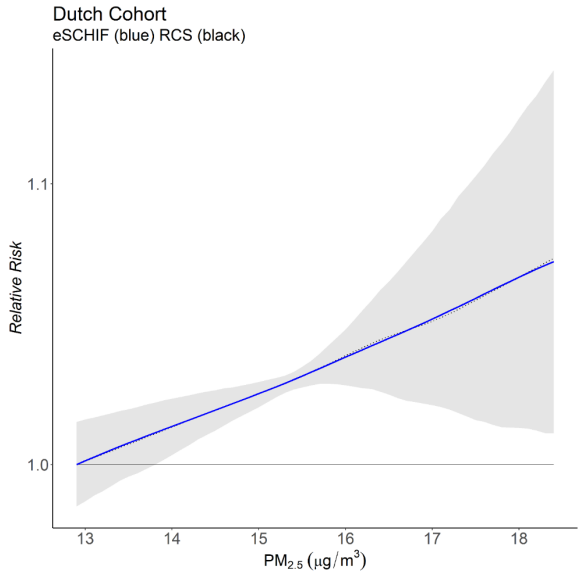
Shape of the $PM_{2.5}$-mortality exposure-response relationship

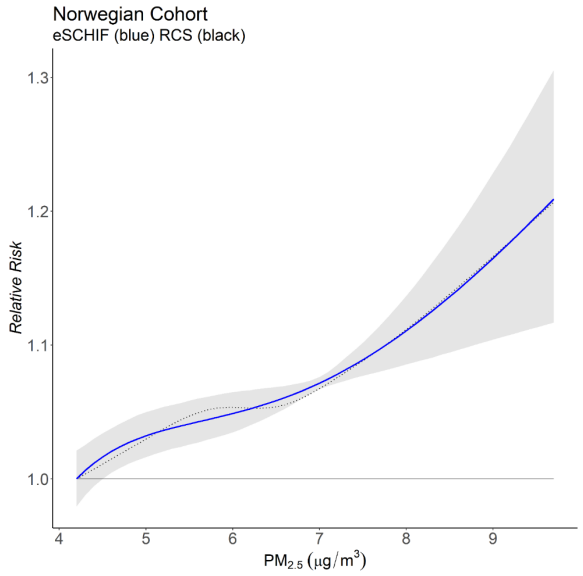


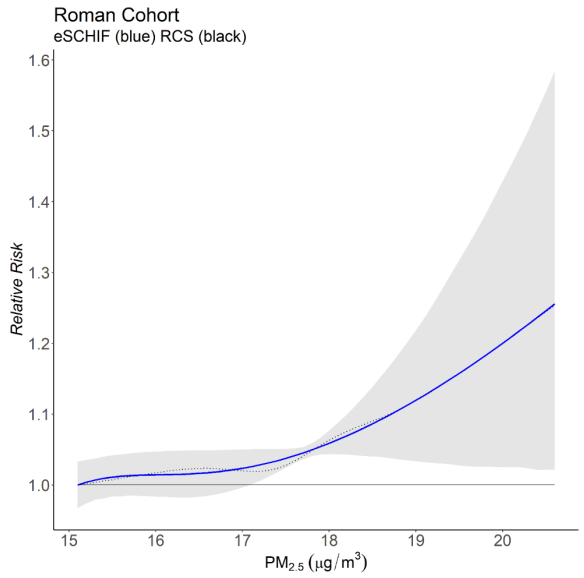


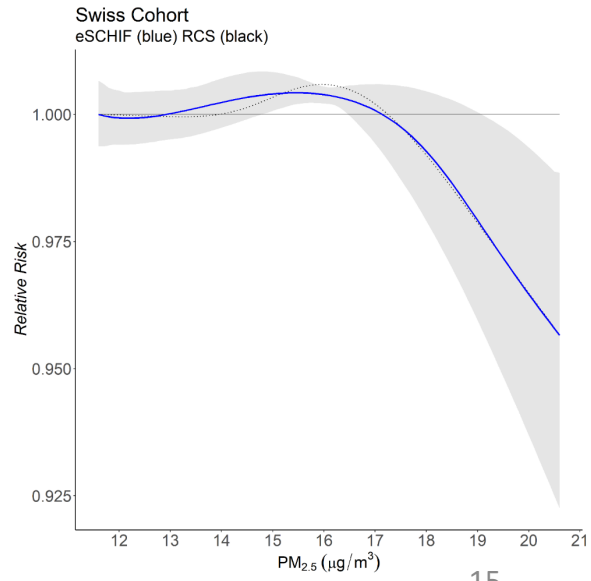


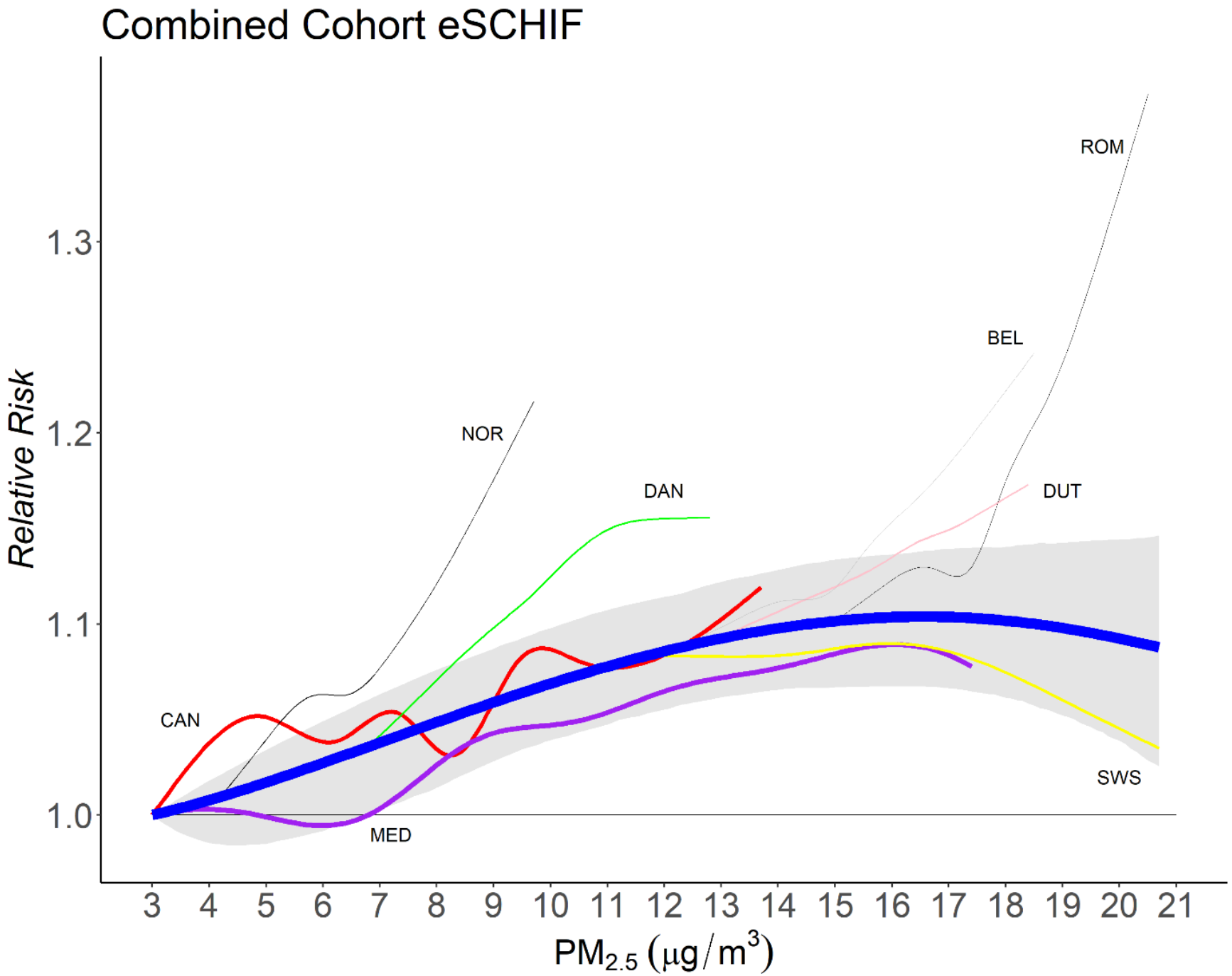











Combined Cohort eSCHIF
Relative Risk
1.0
1.1
1.2
1.3
3
4
5
6
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9
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11
12
13
14
15
16
17
18
19
20
21
PM2.5 (µg/m3)
ROM
BEL
NOR
DAN
DUT
CAN
SWS
MED

SUMMARY

- Applying a harmonized analytical approach marginally reduced the differences in the observed associations across studies; full harmonization was not possible
- Age of the study population, confounders adjusted for, exposure assessment methodology applied all impacted the magnitude of the observed associations, but positive associations were observed in all cases;
- HRs increased in all three studies with more stringent covariate controls
- Shape of the concentration-response relationship differed between cohorts, but generally showed associations down to the lowest observed levels
- A combined eSCHIF suggested a near linear relationship that flattens out at higher concentrations

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Ben Sabbath

Joel Schwartz

Xiao Wu

Antonella Zanobetti

Poster session this afternoon!

1. Harmonized confounder model analyses
2. The shape of the $PM_{2.5}$-mortality exposure-response relationship
3. Harmonized causal inference analyses

ELAPSE

MAPLE

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