

Short-term and long-term health effects of ultrafine particles

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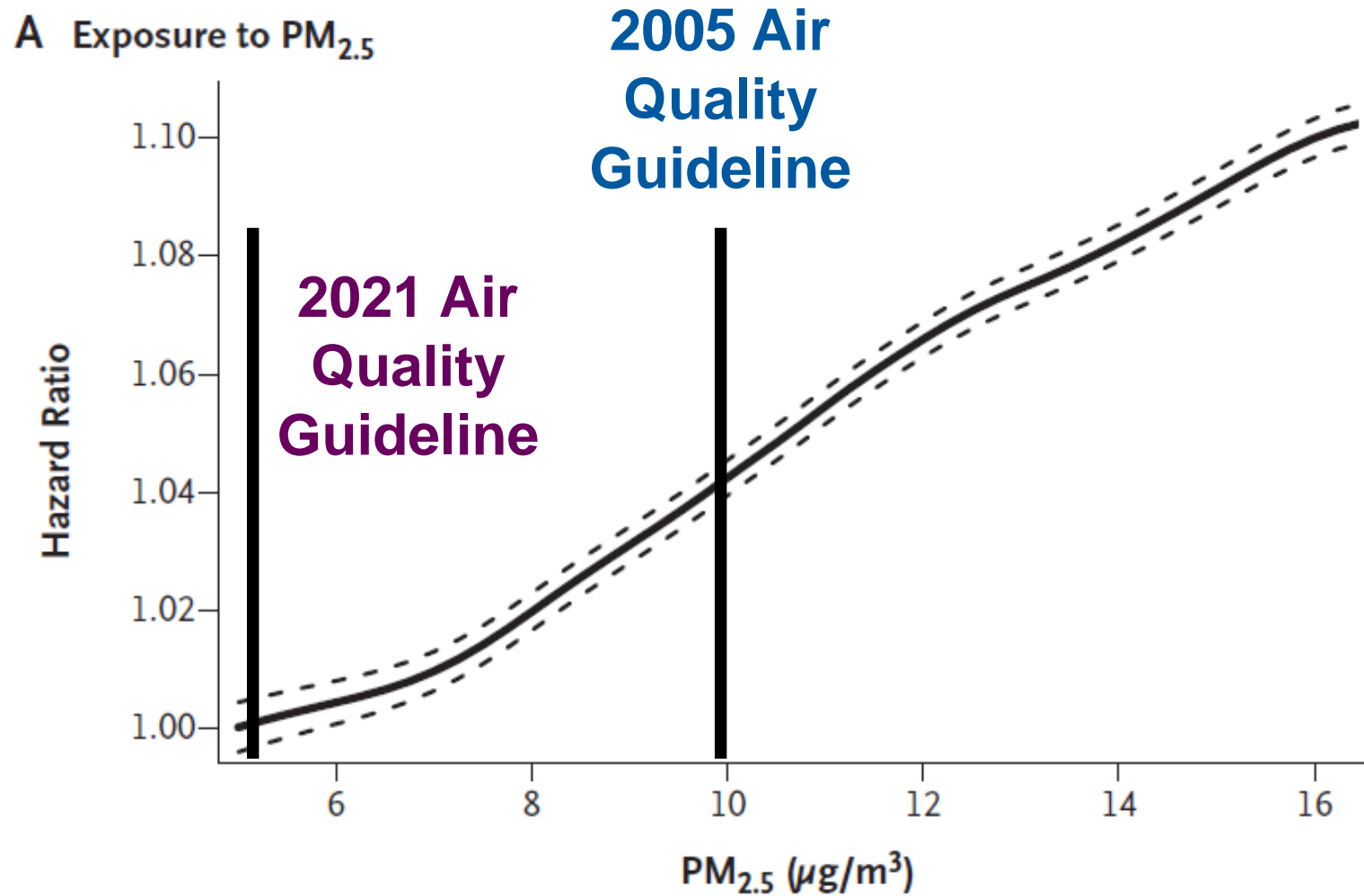
July 4, 2024

↳ Air Pollution is impacting health globally

Harmful Environment

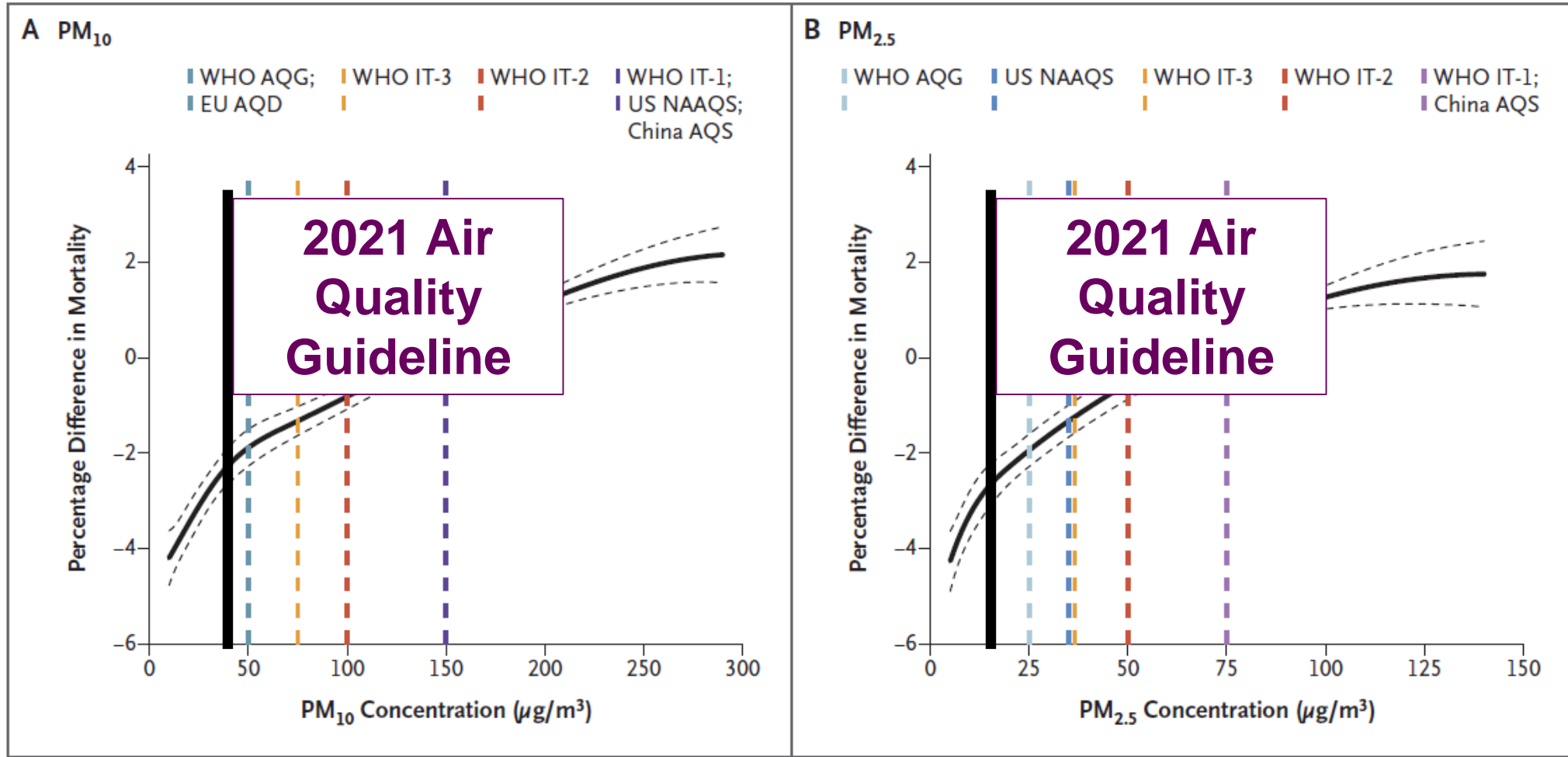


PM_{2.5} and mortality – long-term impacts



Di et al. NEJM 2017

PM_{2.5} and mortality – short-term impacts



Urgent need for action in Europe

		WHO 2005 Air Quality Guidelines	WHO 2021 Air Quality Guidelines	EU Air Quality Directives – Limit Values
PM_{2.5}	Annual	10 µg/m ³	5 µg/m ³	25 µg/m ³
PM_{2.5}	Daily (24-hour)	25 µg/m ³	15 µg/m ³	-
PM₁₀	Annual	20 µg/m ³	15 µg/m ³	40 µg/m ³
PM₁₀	Daily (24-hour)	50 µg/m ³	45 µg/m ³	50 µg/m ³
NO₂	Annual	40 µg/m ³	10 µg/m ³	40 µg/m ³
NO₂	Daily (24-hour)	-	25 µg/m ³	50 µg/m ³

WHO Good Practice Statement on Ultrafine Particles (UFP)

1. Quantify ambient UFP as Particle Number Concentration (PNC) with a lower limit ≤ 10 nm.
2. Expand air quality monitoring strategy by integrating UFP monitoring into the existing air quality monitoring.
3. Distinguish between low and high PNC to guide decisions on the priorities of UFP source emission control.

Low PNC: $< 1\ 000$ particles/cm³ (24-hour mean).
High PNC $> 10\ 000$ particles/cm³ (24-hour mean).
4. Advance the assessment of exposure to UFP for application in epidemiological studies and UFP management.



➔ What do we know about health effects of ultrafine particles?

Health Effects Institute Review

HEI Perspectives 3

January 2013

Insights from HEI's research



Understanding the Health Effects of Ambient Ultrafine Particles

HEI Review Panel on Ultrafine Particles

Systematic Literature Review

International Journal of Public Health (2019) 64:547–559

<https://doi.org/10.1007/s00038-019-01202-7>



REVIEW



Health effects of ultrafine particles: a systematic literature review update of epidemiological evidence

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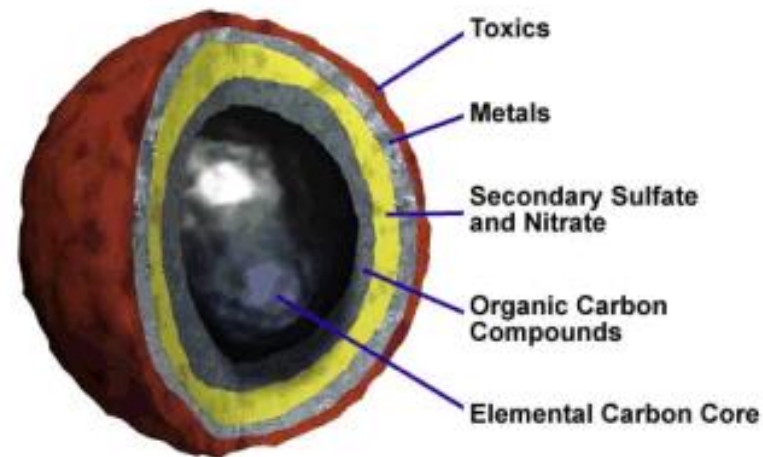
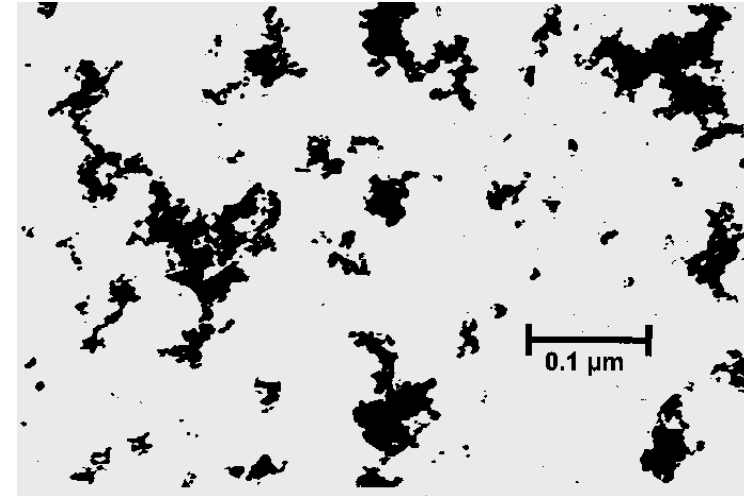
Ultrafine Particles and Health – Epidemiological Evidence

	1997-2011	2011-2017	Sum
Long-term Exposure			
Mortality	0	1	1
Morbidity	0	4	4
Emergency/hospital call/admission	0	0	0
Subclinical	0	5	5
All	0	10	10
Short-term Exposure			
Mortality	11	7	18
Morbidity/ Emergency/hospital call/admission	15	5	20
(Respiratory) Symptoms	8	11	19
Subclinical	52	55	107
All	86	78	164
Total	86	88	174

⇒ Particle properties
determine the health
effects

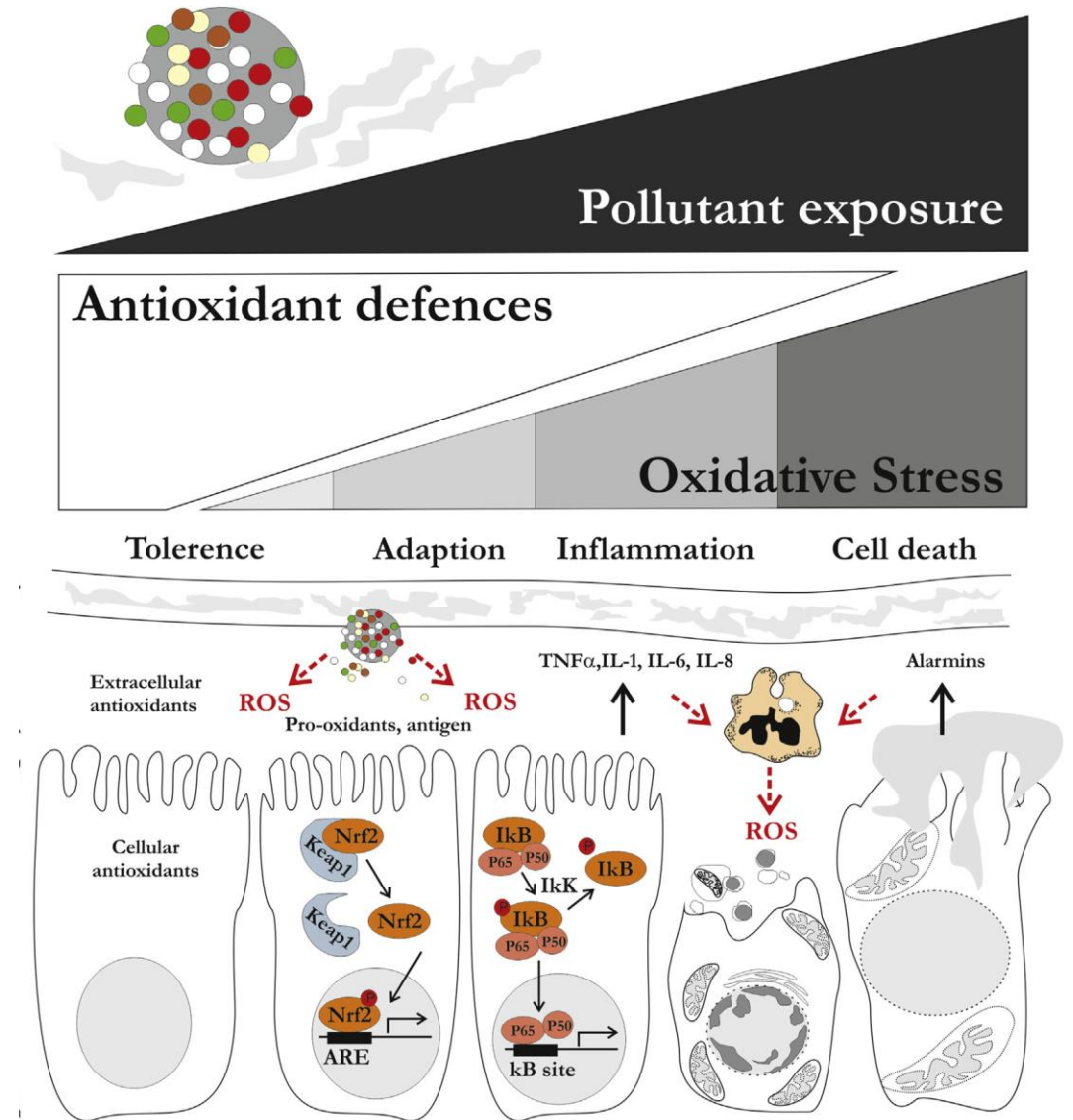
Particle properties related to health effects

- Fine particles
- Coarse particles
- Ultrafine particles
- Particle composition
 - Black carbonaceous particles
 - Secondary organic aerosols
 - Secondary inorganic aerosols



Lung – First line of defense

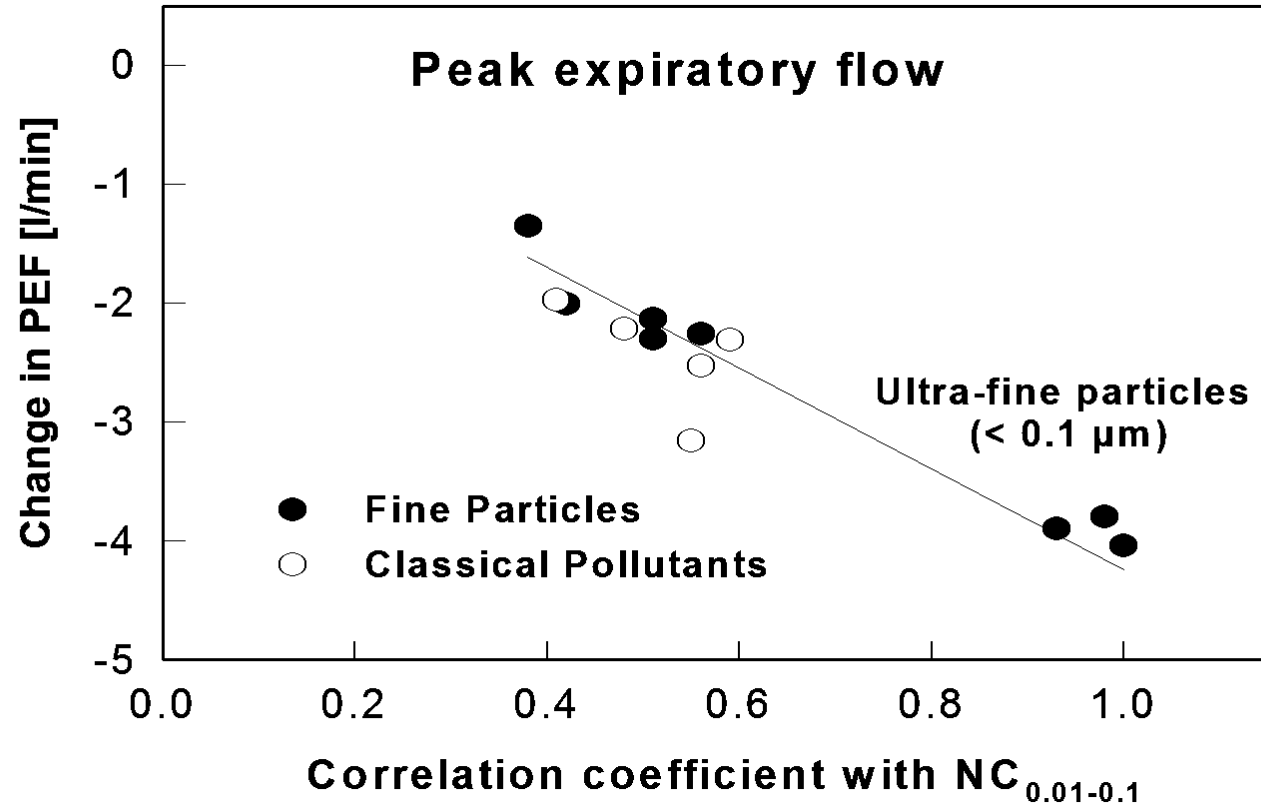
- All regulated air pollutants exhibit oxidative stress
- Air pollution impairs lung growth and functioning and contributes to lung diseases
- Lung health is essential for responding to and mitigating the health impacts of air pollutants

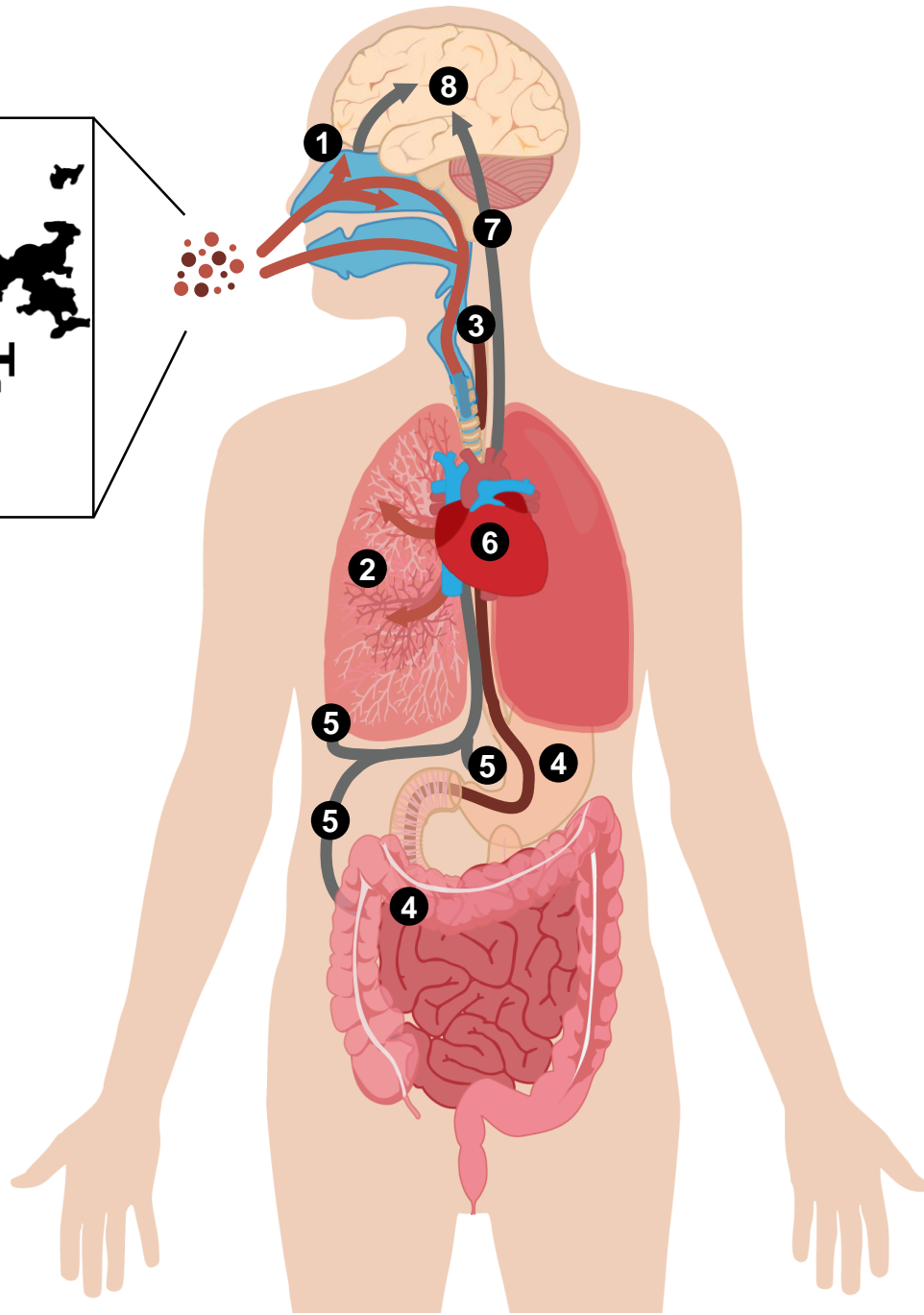
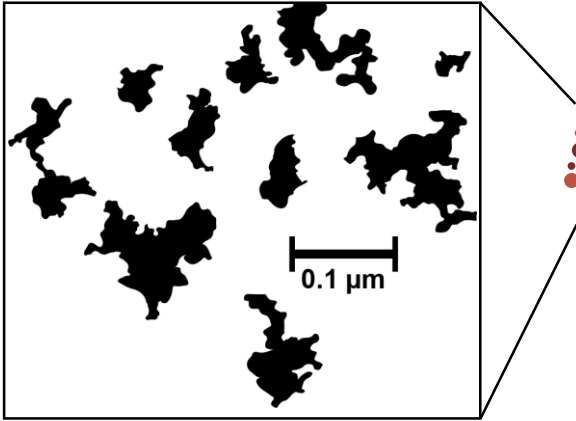


Where it all started: Panel Study in Asthmatics



Decreased lung function on days with high ultrafine particles





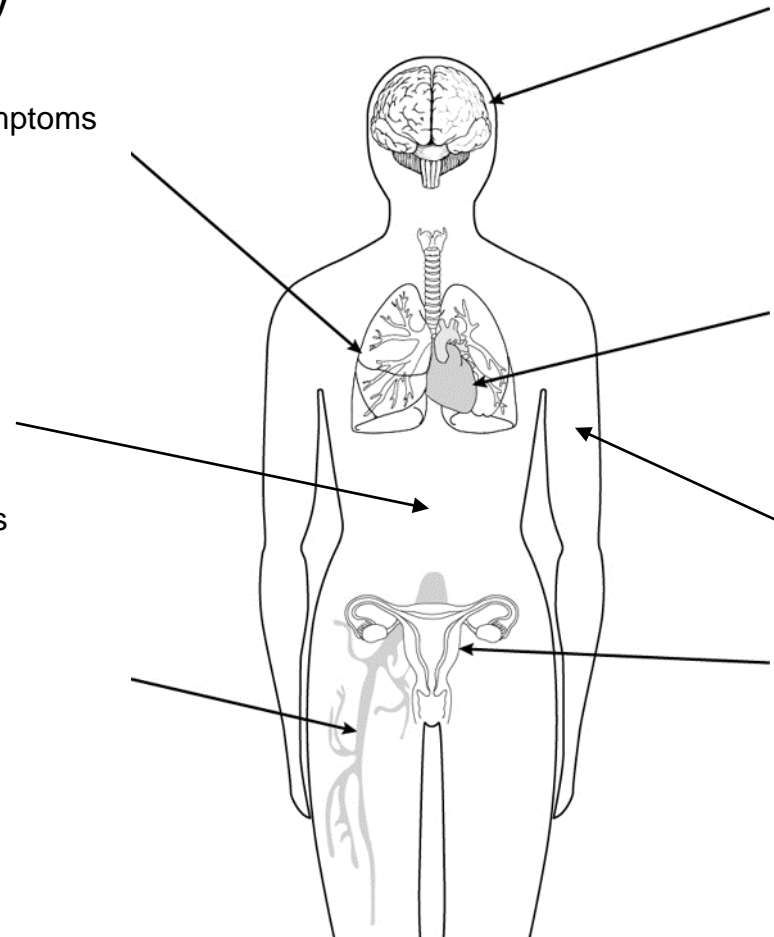
- 1 Ultrafine particles (UFP) deposited in the nasal cavity translocate to the brain via the olfactory nerve
- 2 Particles deposited in the lung activate the immune system
- 3 Particles are swallowed after clearance from the lung or deposition in the upper airways
- 4 Particles reach the gastrointestinal tract
- 5 UFP and constituents translocate into the blood stream
- 6 UFP and constituents passage the heart
- 7 UFP and constituents from different organs reach the brain vasculature
- 8 UFP and constituents induce localized and diffuse inflammatory responses, protein misfolding, glial and vascular dysfunction, and neuronal degradation leading to different forms of dementia

Local and Systemic Health Effects of Air Pollution

- **Respiratory Disease Mortality**
- **Respiratory Disease Morbidity**
- **Lung Cancer**
- **Pneumonia**
- Upper and lower respiratory symptoms
- Airway inflammation
- Decreased lung function
- Decreased lung growth

- Insulin Resistance
- **Type 2 diabetes**
- **Type 1 diabetes**
- Bone metabolism
- Liver functioning
- Liver and digestive tract cancers

- **High blood pressure**
- Endothelial dysfunction
- Increased blood coagulation
- Systemic inflammation
- **Deep Venous Thrombosis**



- **Stroke**
- Neurological development
- Mental Health
- **Neurodegenerative diseases**

- **Cardiovascular Disease Mortality**
- **Cardiovascular Disease Morbidity**
- **Myocardial Infarction**
- **Arrhythmia**
- **Congestive Heart Failure**
- Changes in Heart Rate Variability
- ST-Segment Depression

- Skin Aging

- **Premature Birth**
- **Decreased Birth Weight**
- Decreased foetal growth
- In uterine growth retardation
- Decreased sperm quality
- Preclampsia

Thurston et al. ERJ 2017 (modified)

↳ Ultrafine particles impair health in vulnerable subgroups

Times spent in traffic and triggering of myocardial infarction one hour later

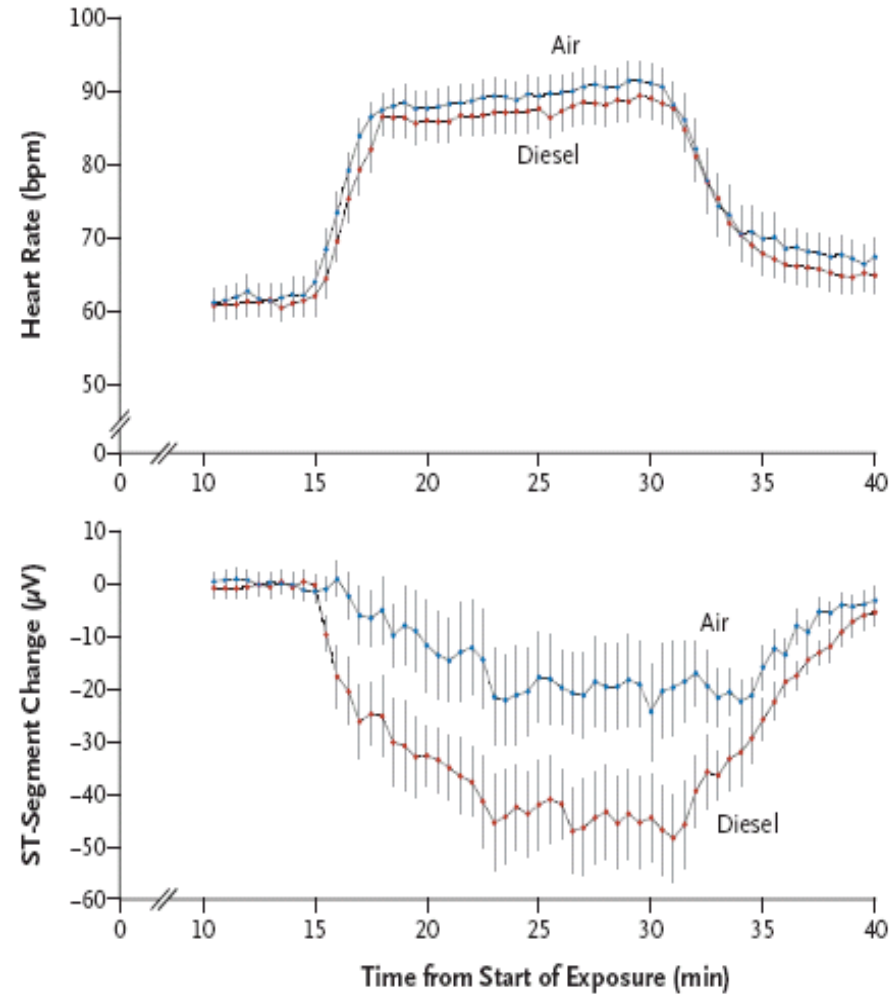


	All	Cars	Bus/Tram	Bicycle
Odds Ratio*	3.2	3.3	2.9	2.6
95% Confidence-interval	2.7 – 3.9	2.7 – 4.1	1.7 – 5.1	1.6 – 4.1

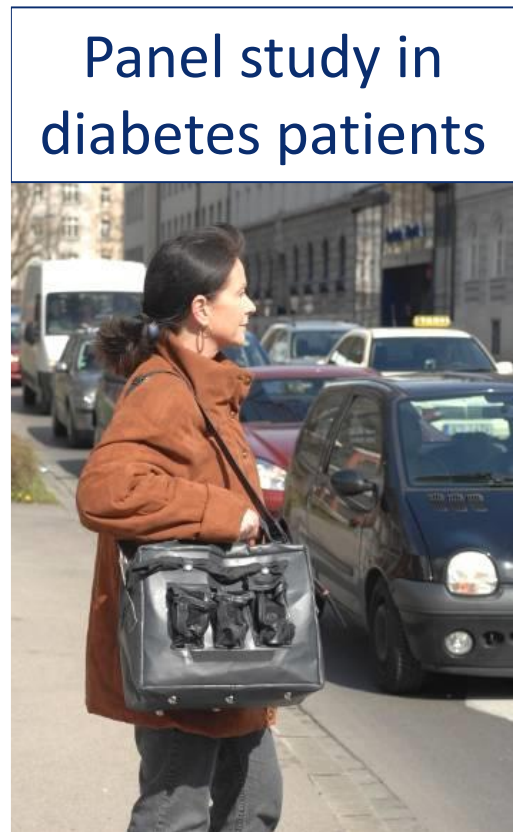
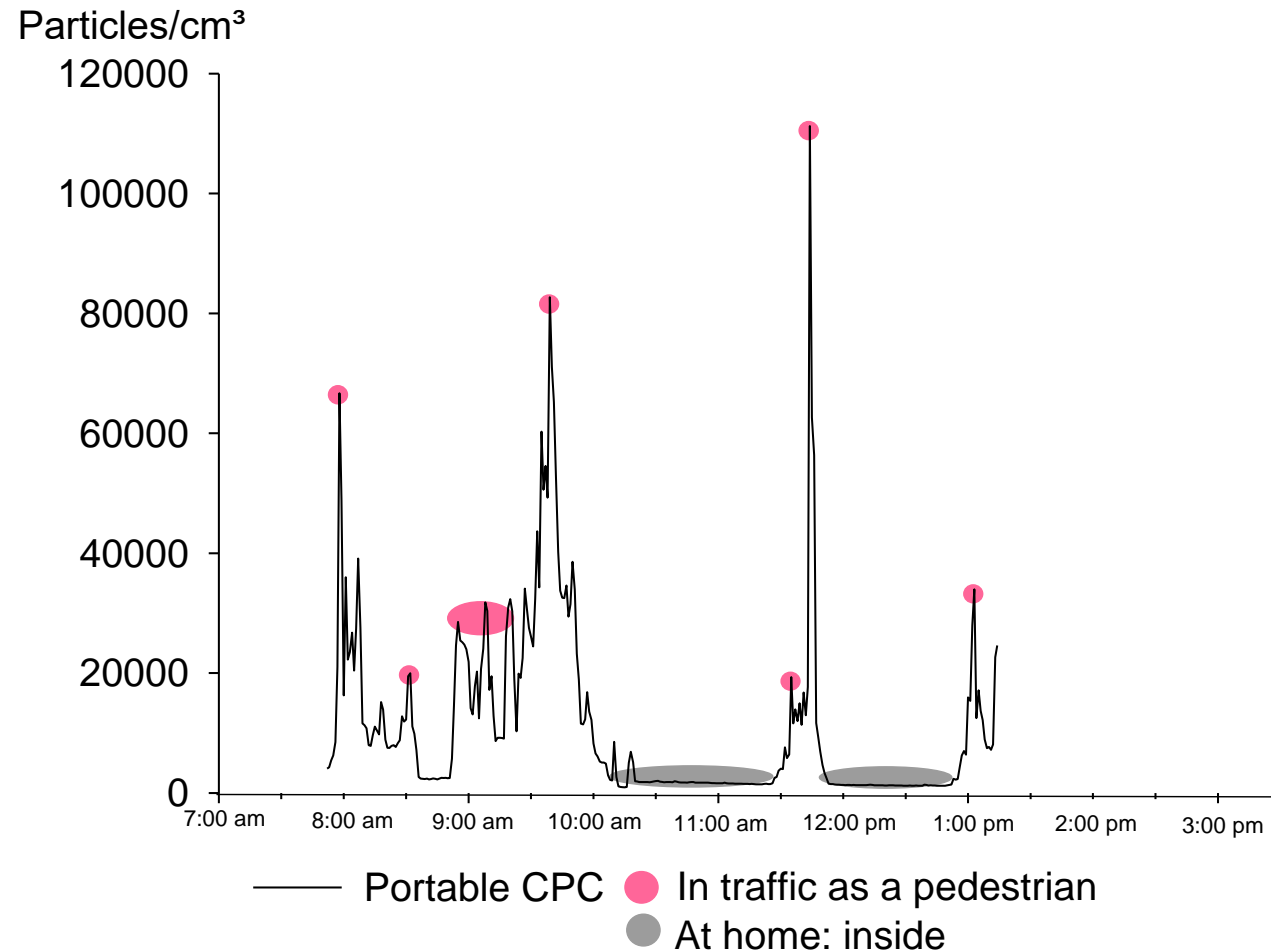
*adjusted for getting up, being outdoors and strenuous exercise

Exposure to diesel exhaust induces ischemia in patients

- Controlled exposure to diesel exhaust; PM concentration: $300\mu\text{g}/\text{m}^3$, $\text{Ø } 54 \text{ nm}$
- 20 men with coronary artery disease, mean age 60
- Ischemic changes in the ECG during exercise
- Reduced tissue plasminogen activator release after 6-8 hours of exposure

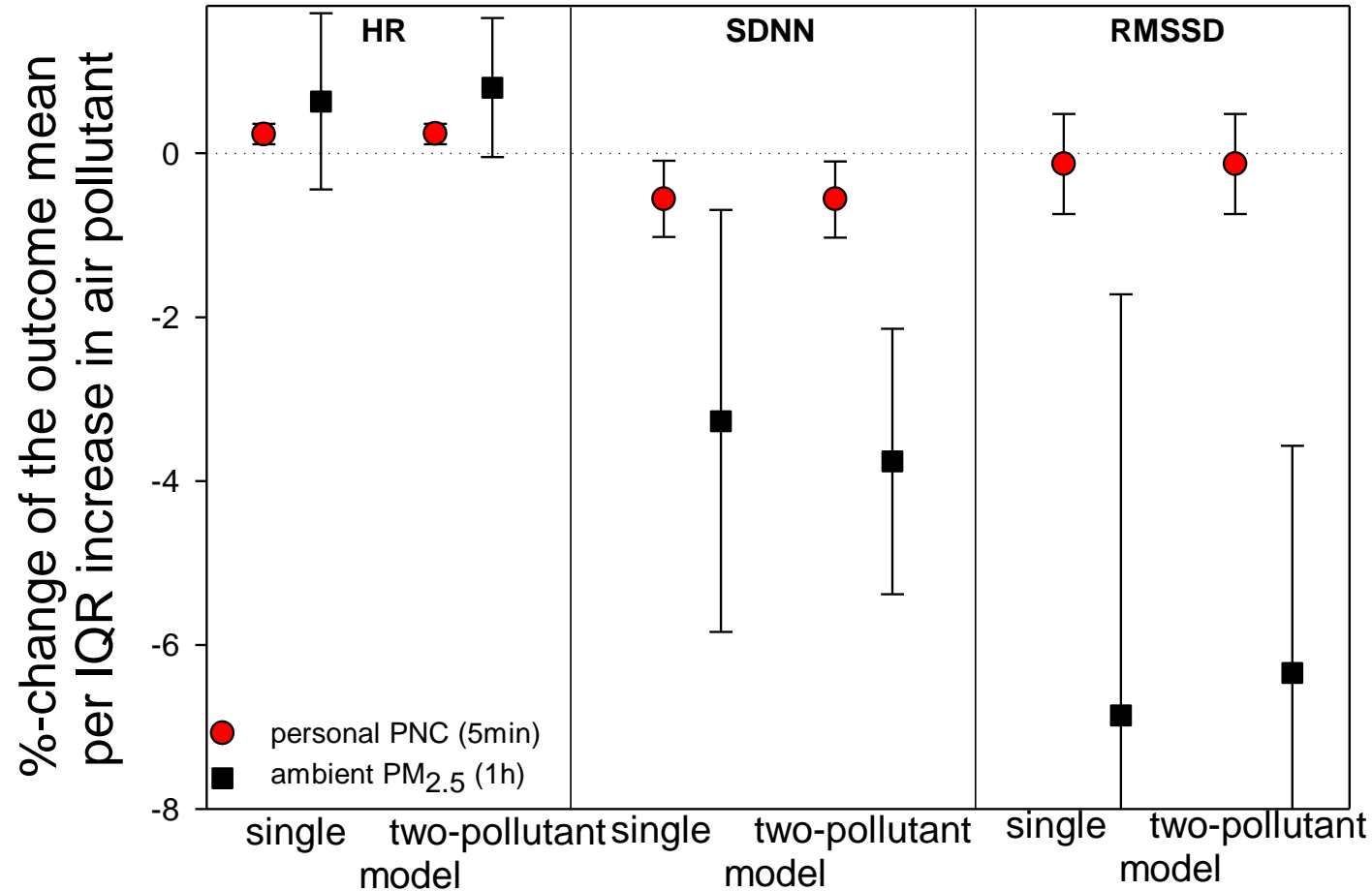


Cardiac Responses and personal UFP exposure



Cardiac Responses and personal UFP exposure

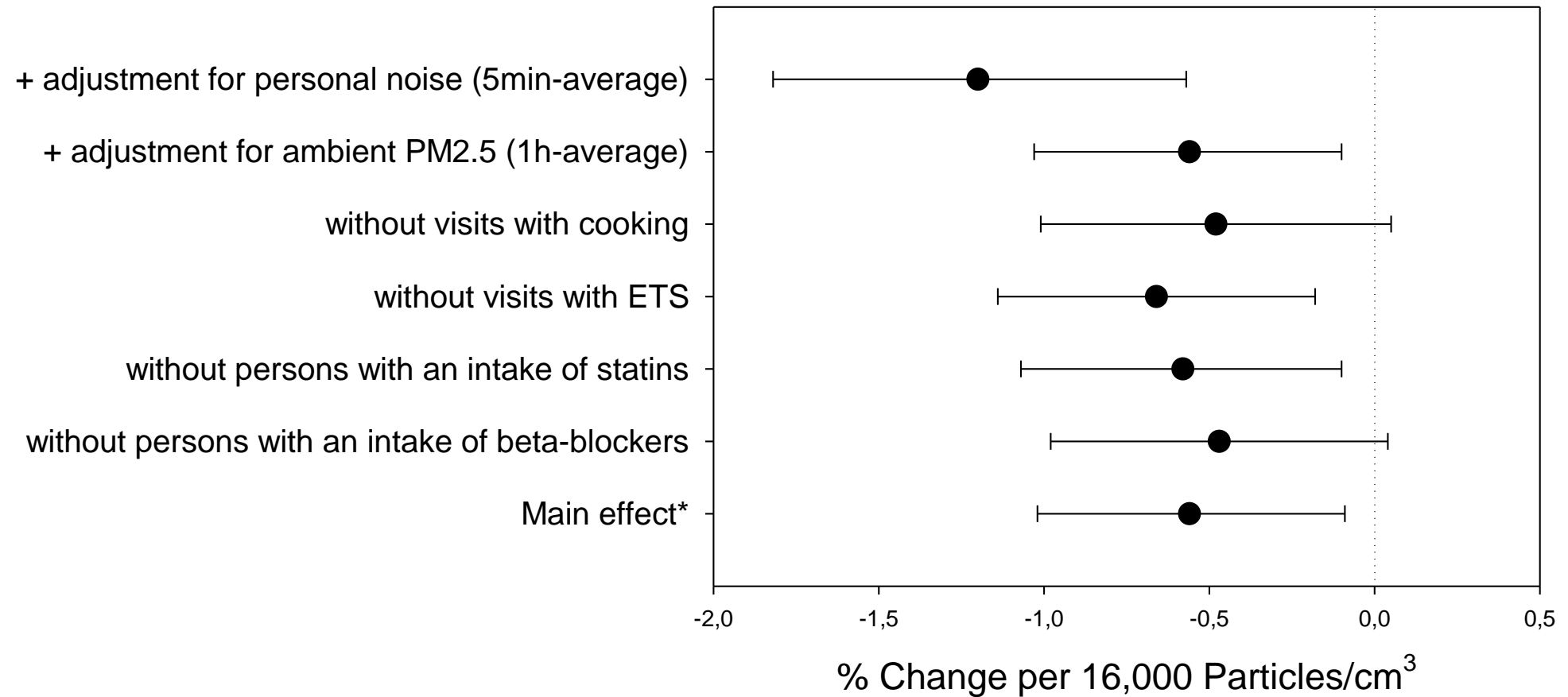
Personal and Central-site Particle Measurements



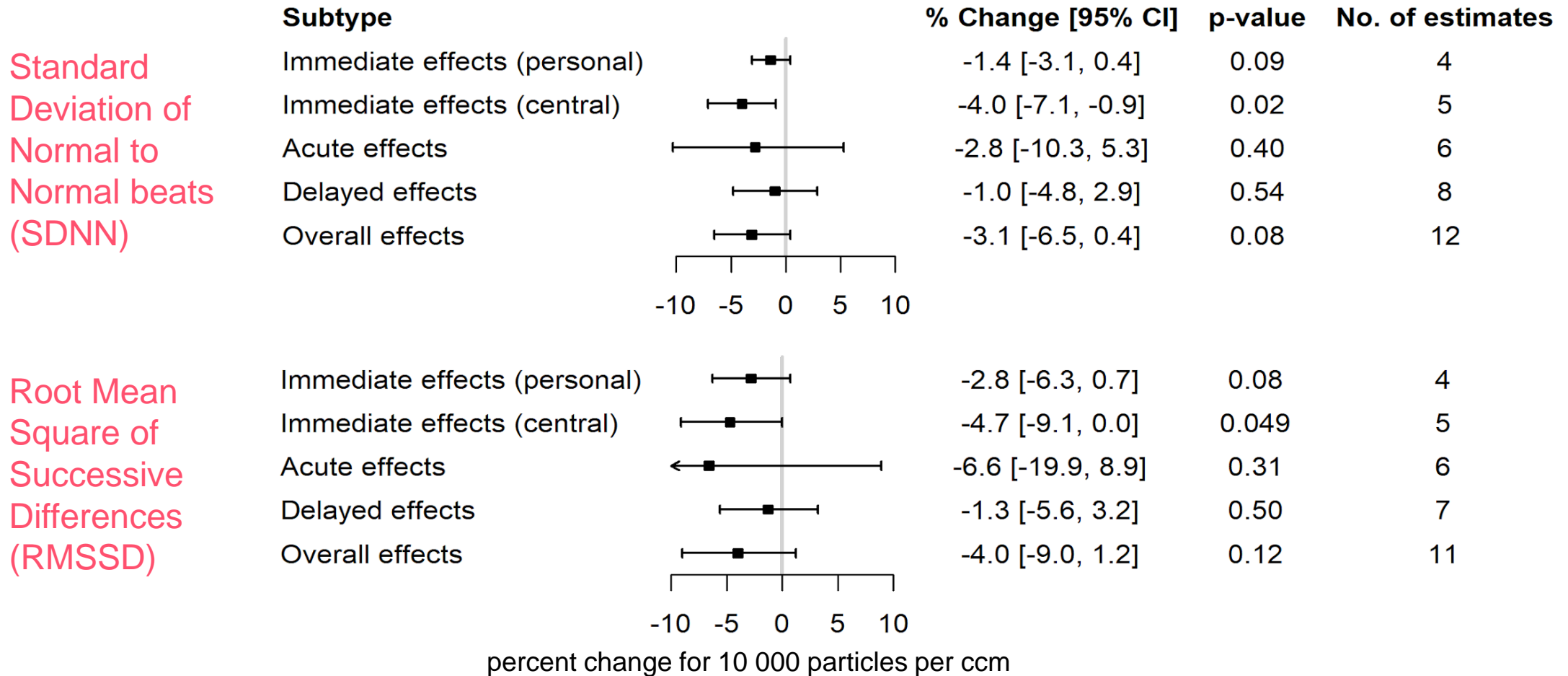
Peters et al. PFT 2015

Heart rate variability and personal UFP exposure

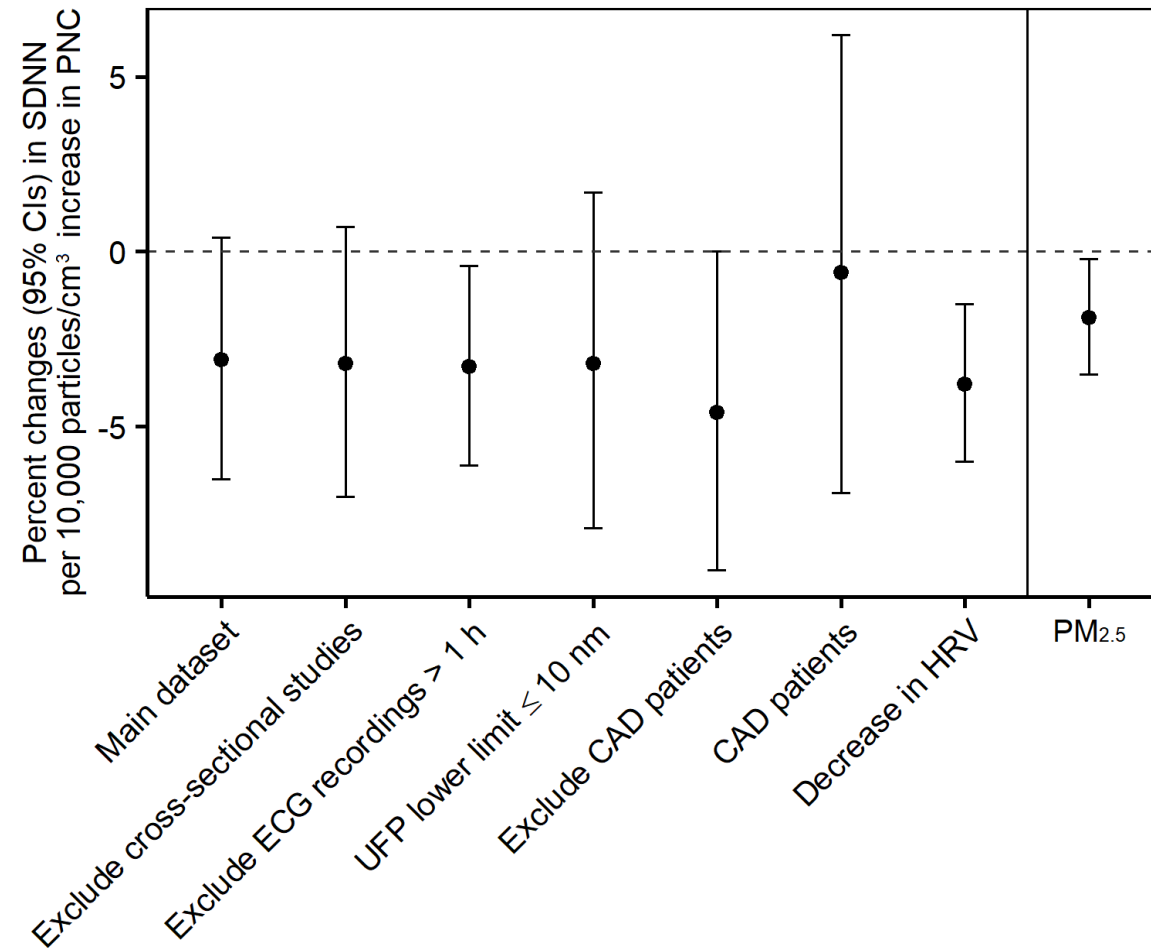
Standard Deviation of Normal to Normal beats (SDNN)



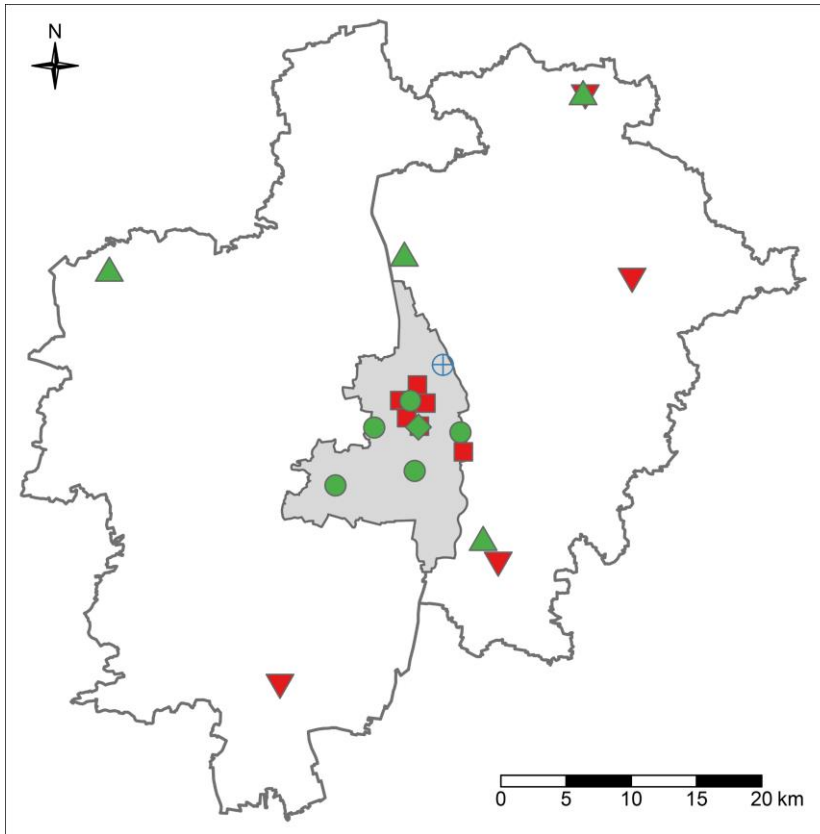
Meta-analyses of UFP and heart rate variability



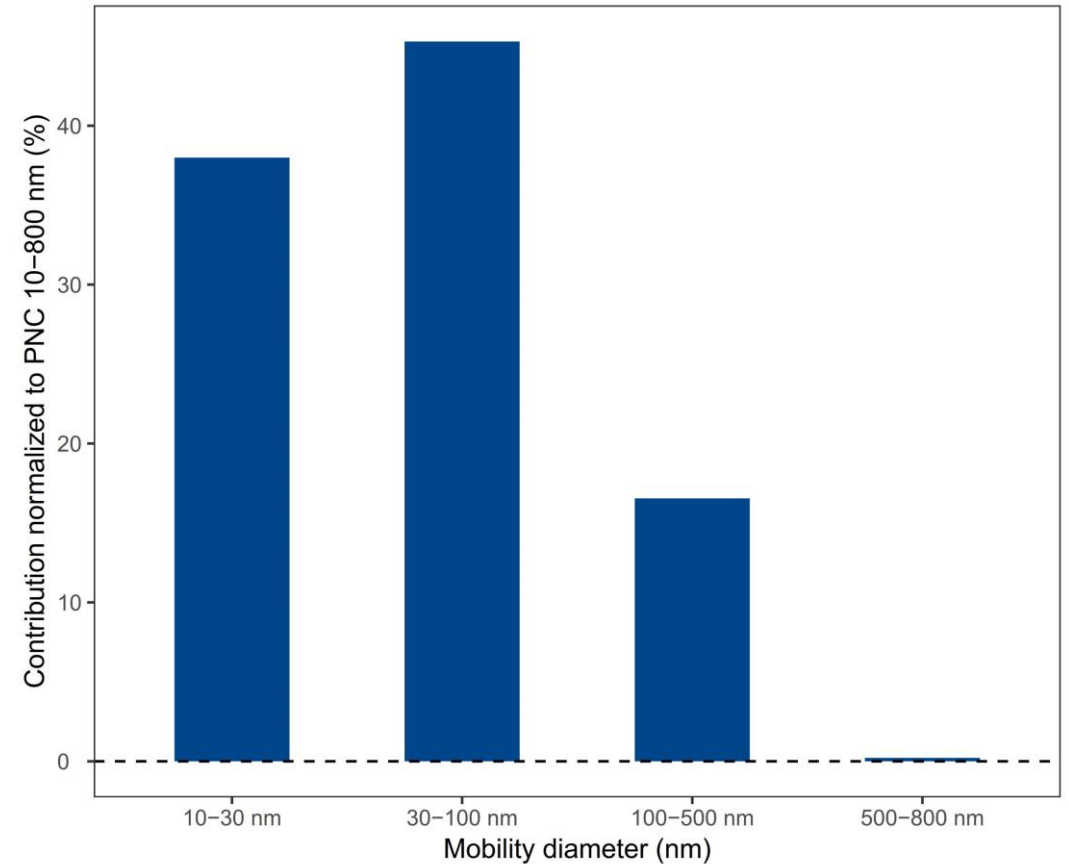
Meta-analyses of UFP and heart rate variability



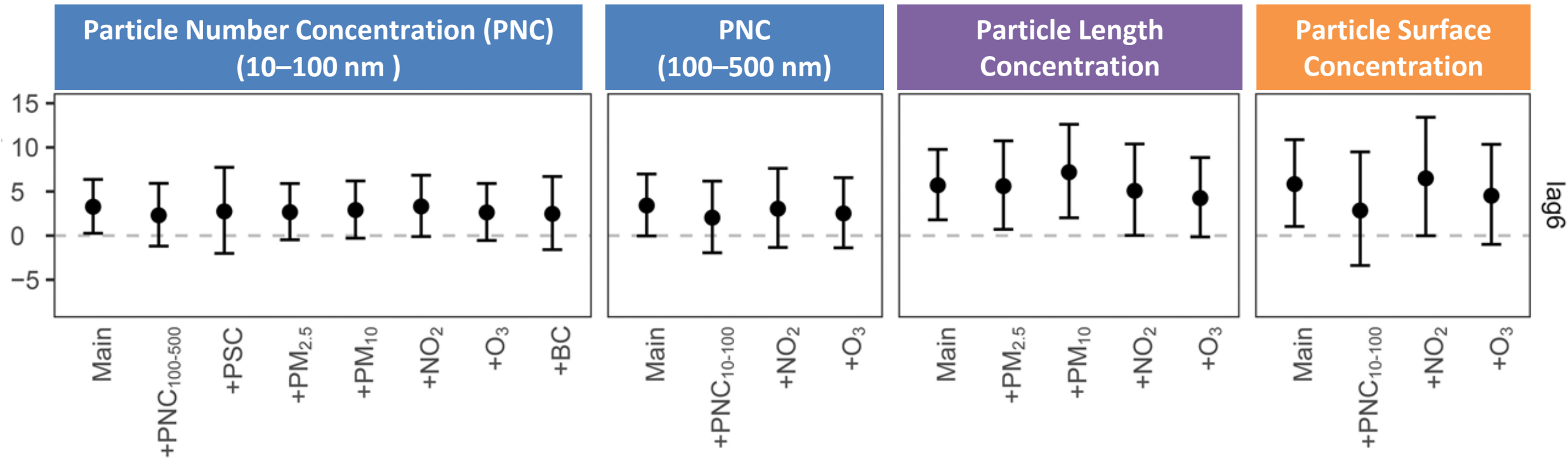
Particle size ranges and contributions to number concentration (10-800 nm) in Augsburg, 2005-2015



- Type of stations**
- ◆ Main station
 - ▲ Regional background
 - ▼ Regional traffic
 - Urban background
 - Urban traffic
 - ⊕ Industry area
- Study area**
- Augsburg city
 - County



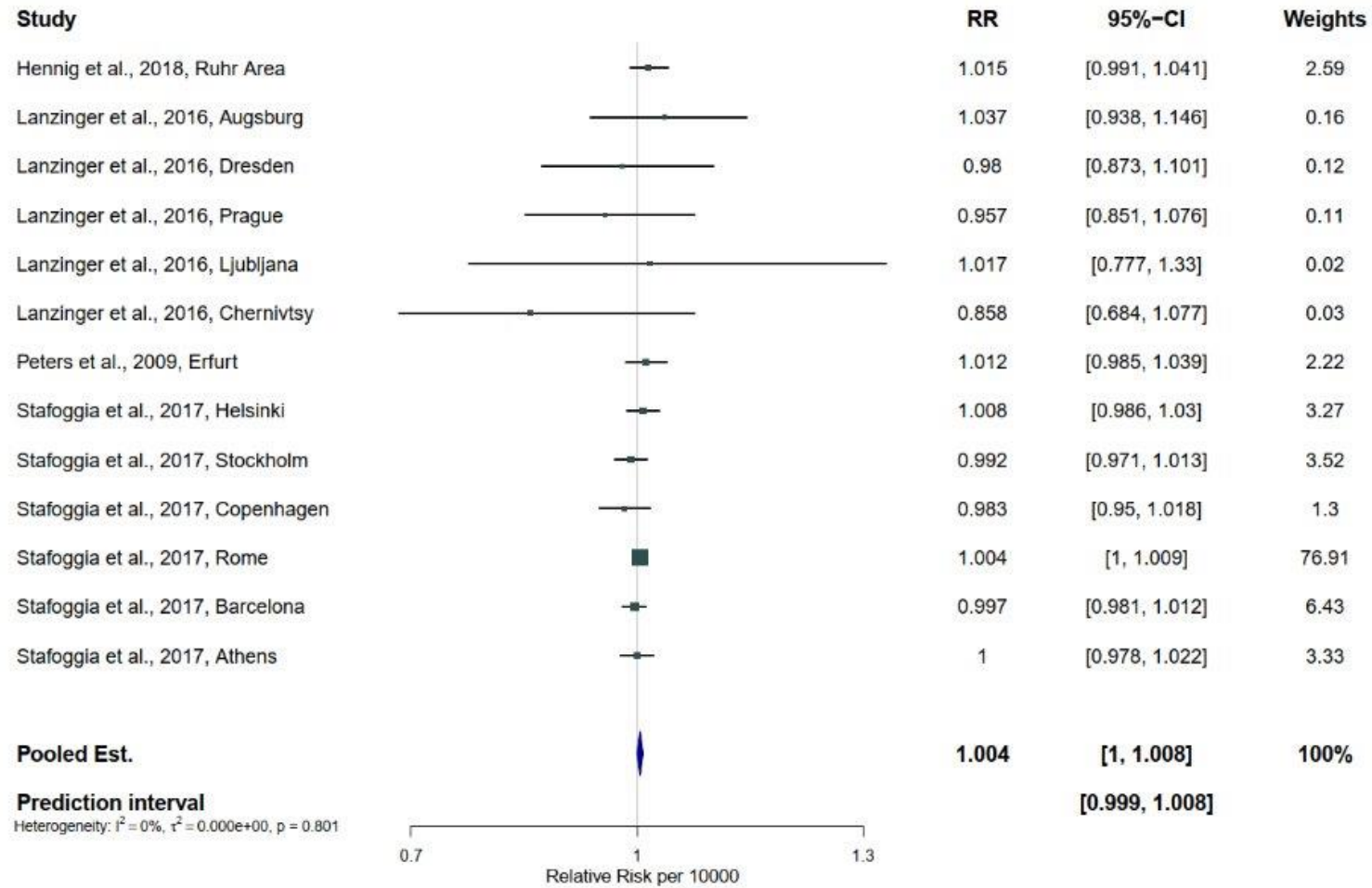
Hourly exposure to ultrafine particle metrics and the onset of myocardial infarction in Augsburg



Percent difference (95% CI) in cases of myocardial infarction per interquartile range (IQR) increase in particle metrics (lag 6 h) with additional adjustment for co-pollutants in Augsburg, Germany from 2005 to 2015.

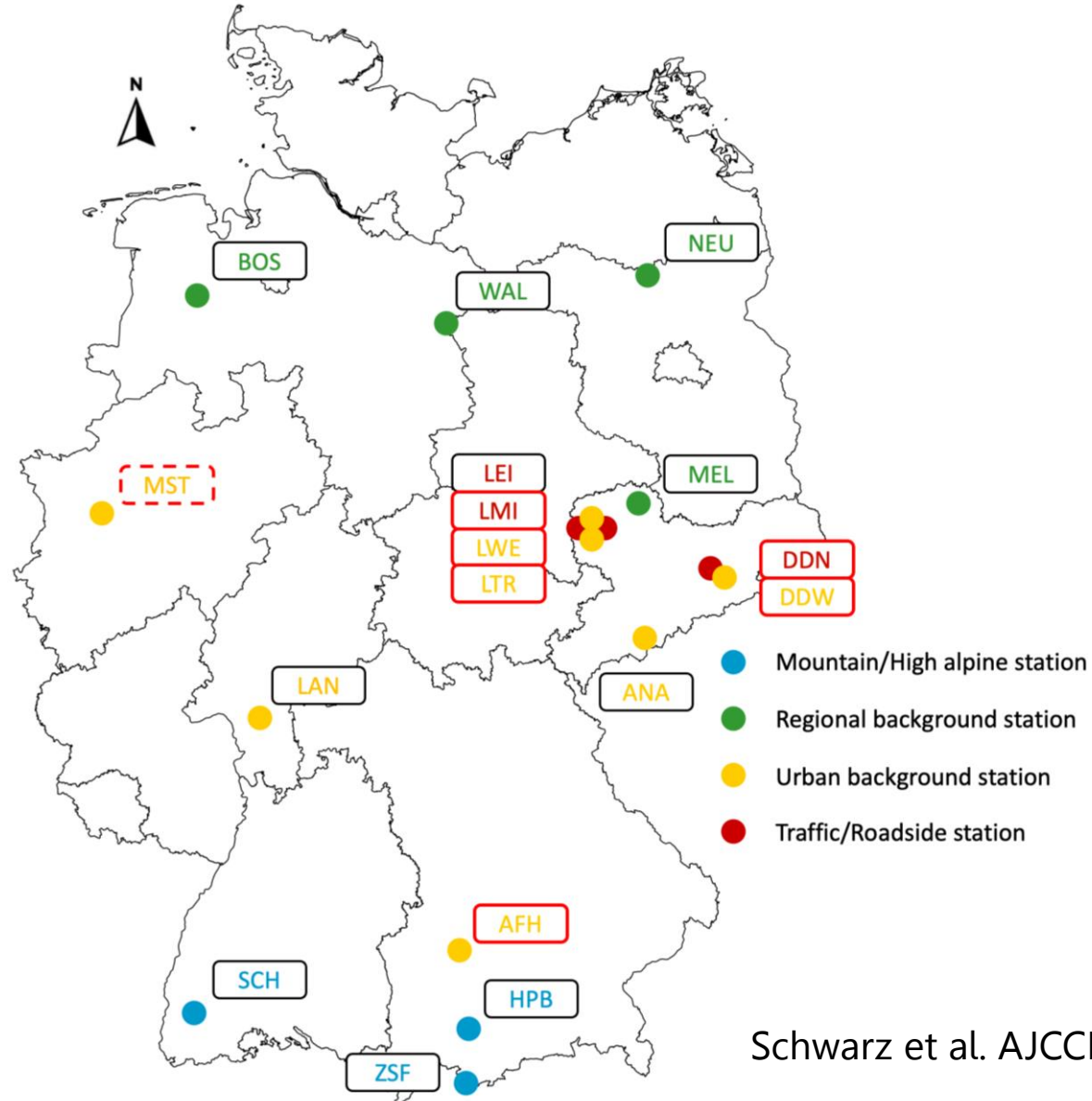
⇒ Daily concentrations of ultrafine particles are linked to mortality

Ultrafine particles and natural mortality



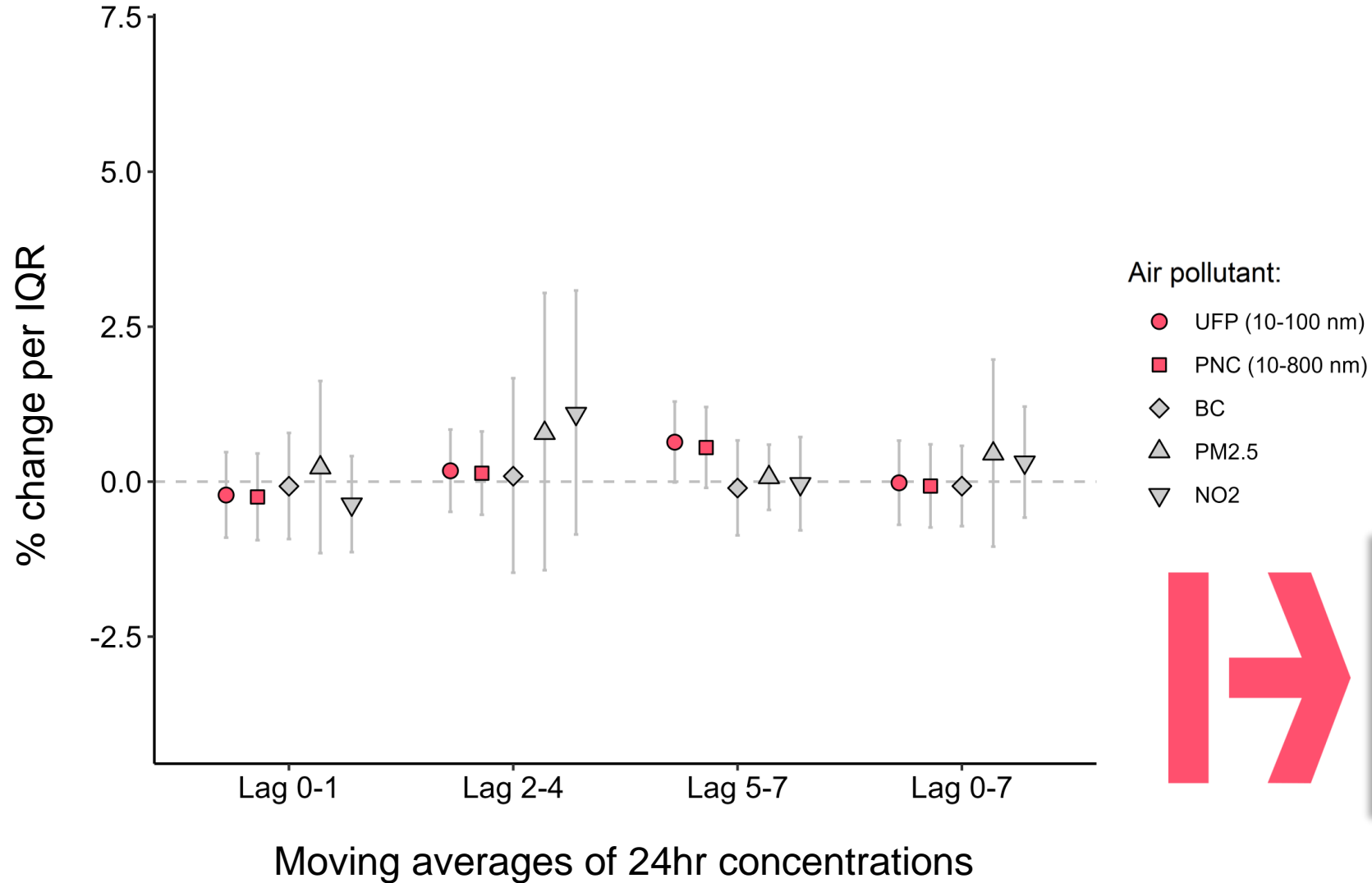
Breitner et al. unpublished

Impact of extended time series of ultrafine particles



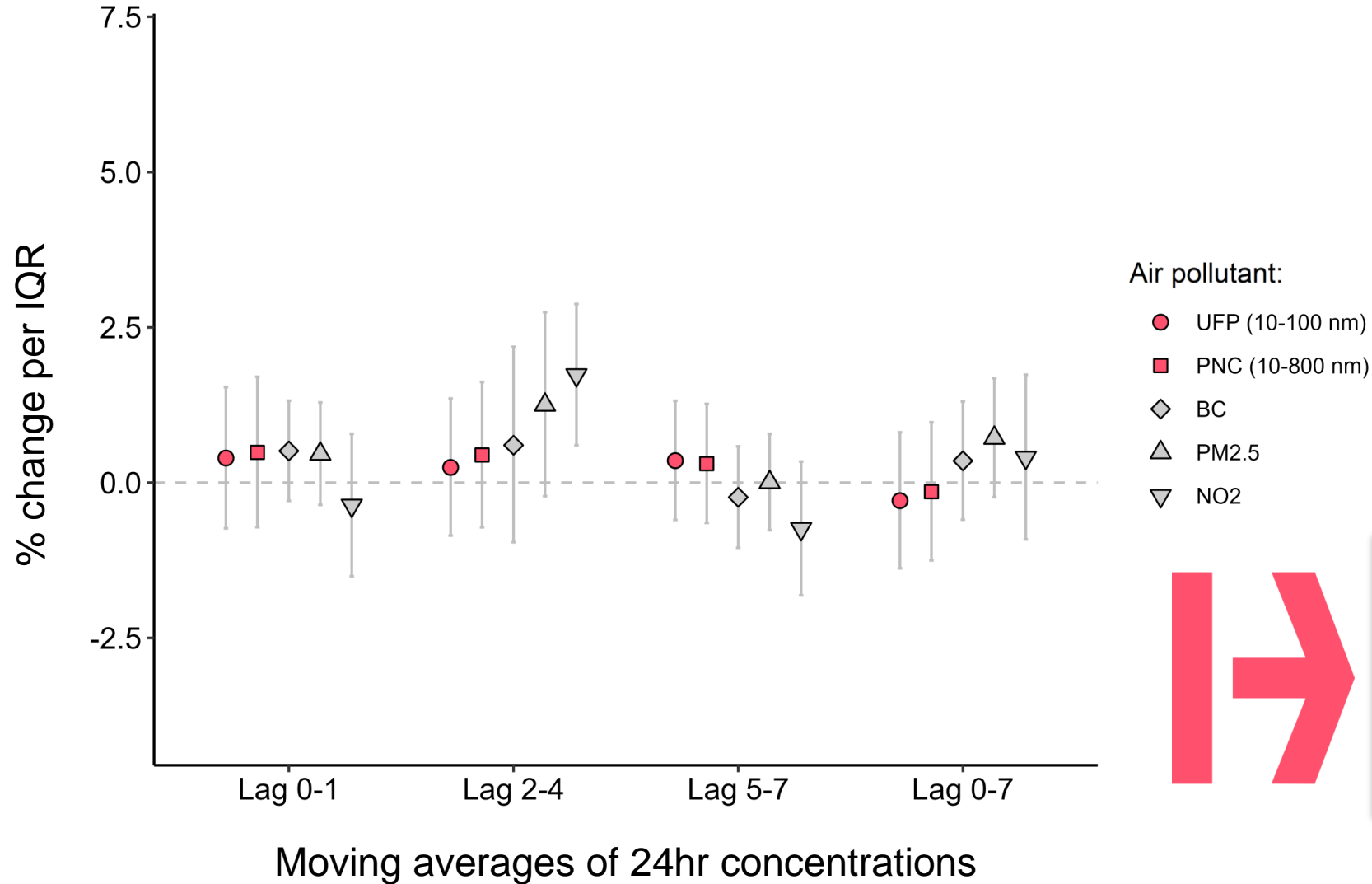
- Multi-center epidemiological time series study between 2010 and 2017
- Six stations that were part of the former German Ultrafine Aerosol Network (GUAN)
- Two-stage modelling design:
 - I. Station-specific confounder adjusted Poisson regression
 - II. Novel multi-level meta-analytical approach for environmental research

Ultrafine particle effects on natural mortality



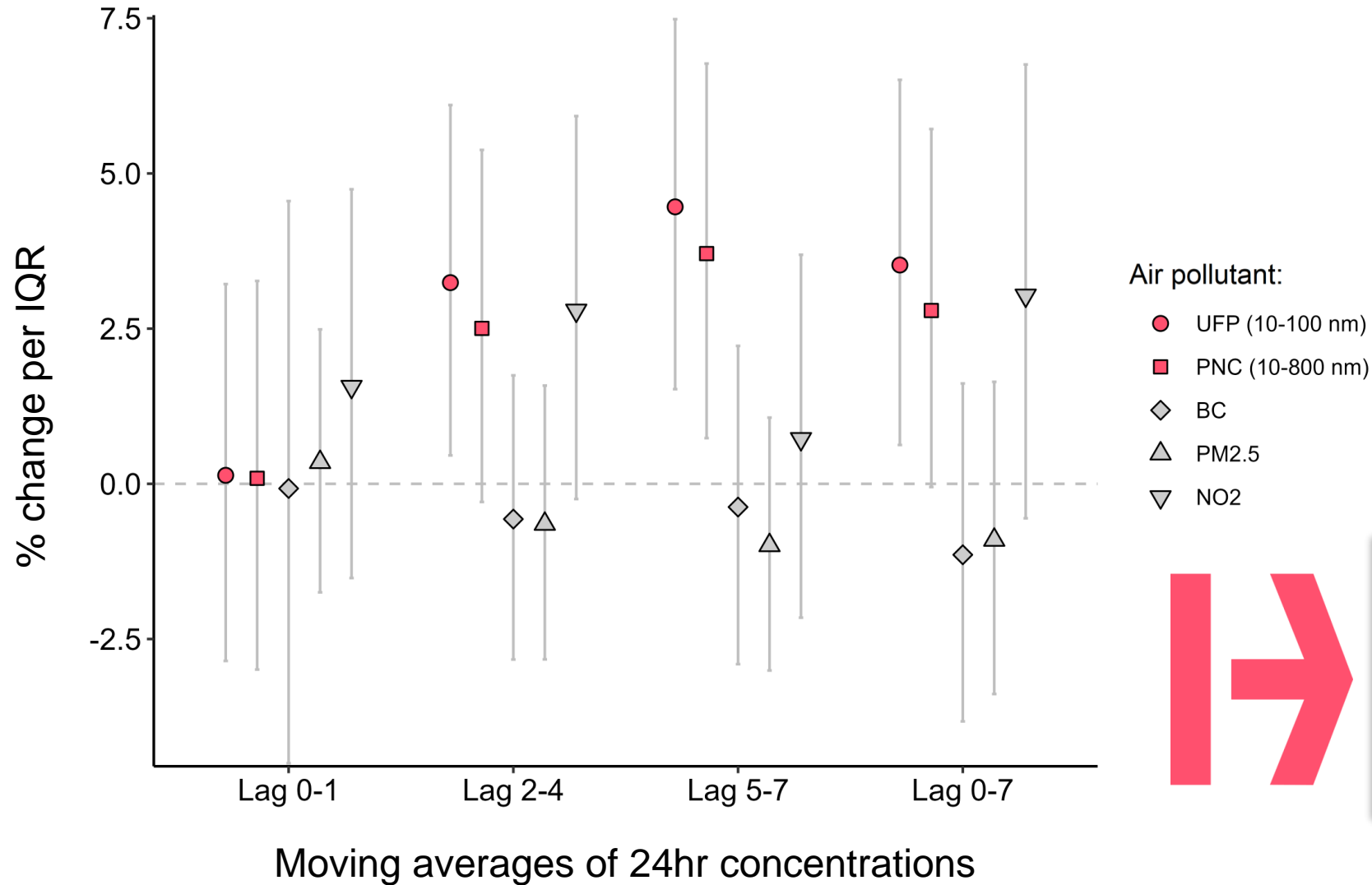
Findings corroborate studies in Erfurt, Germany in the 1990ies

UFP effects on cardiovascular mortality



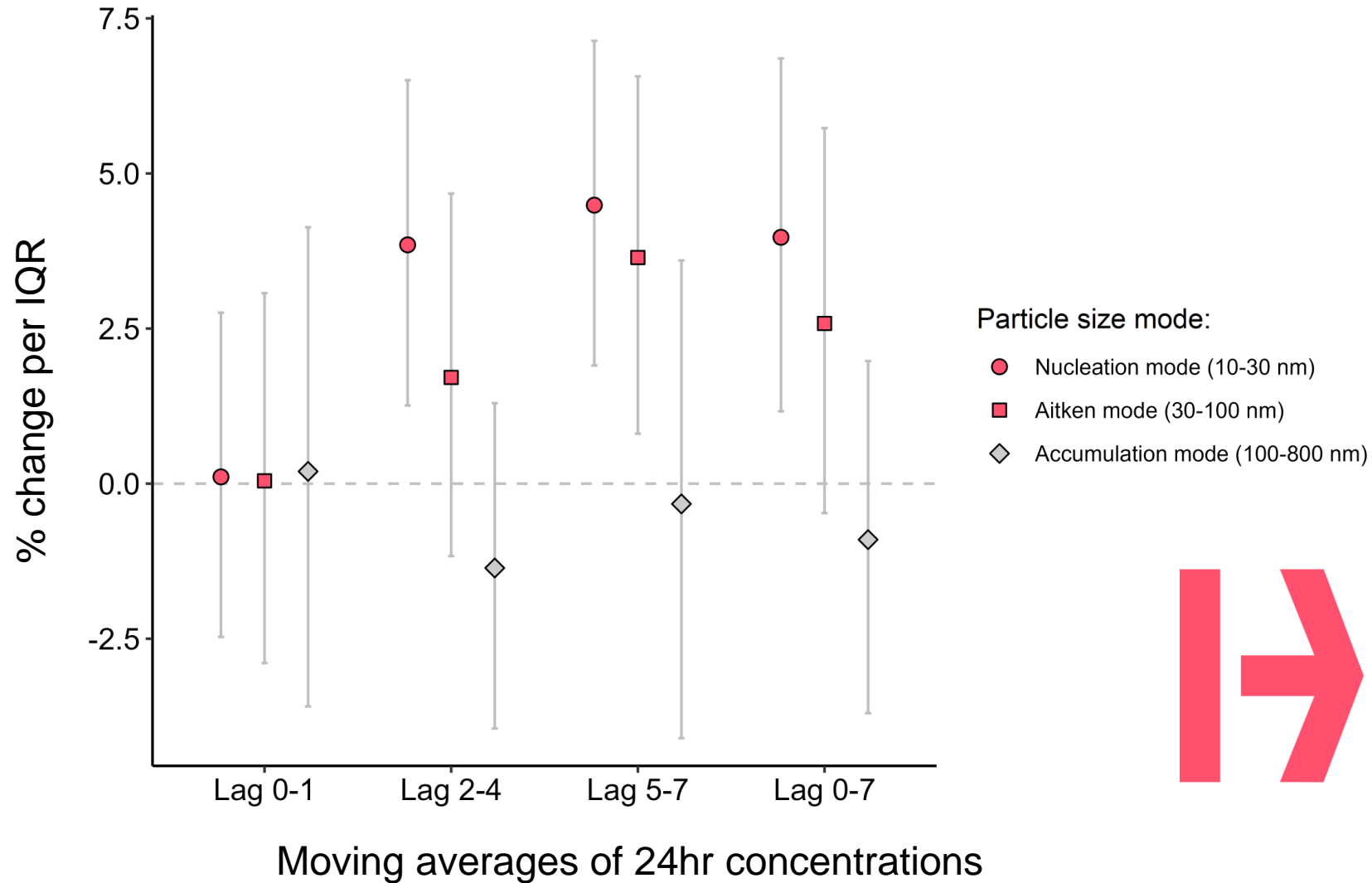
Nitrogen dioxide associated with cardiovascular disease mortality

Ultrafine particle effects on respiratory mortality



**Ultrafine particles
associate with
respiratory mortality
in the 2010s**

UFP effects on respiratory mortality



**Strongest effects
were observed for
the smallest ultrafine
particles**

↳ What about long-term health impacts of ultrafine particles?

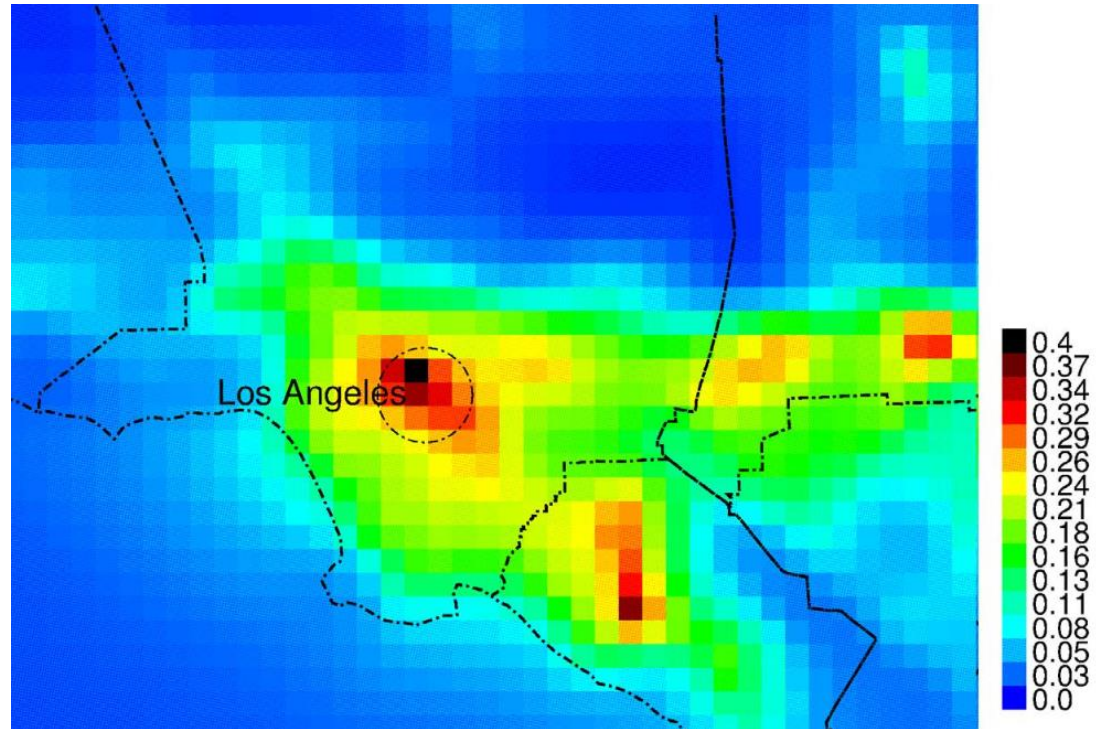
California teachers study – Modelling ultrafines

Exposure estimation for
4km grids based on
emission inventories

Mass, species and sources

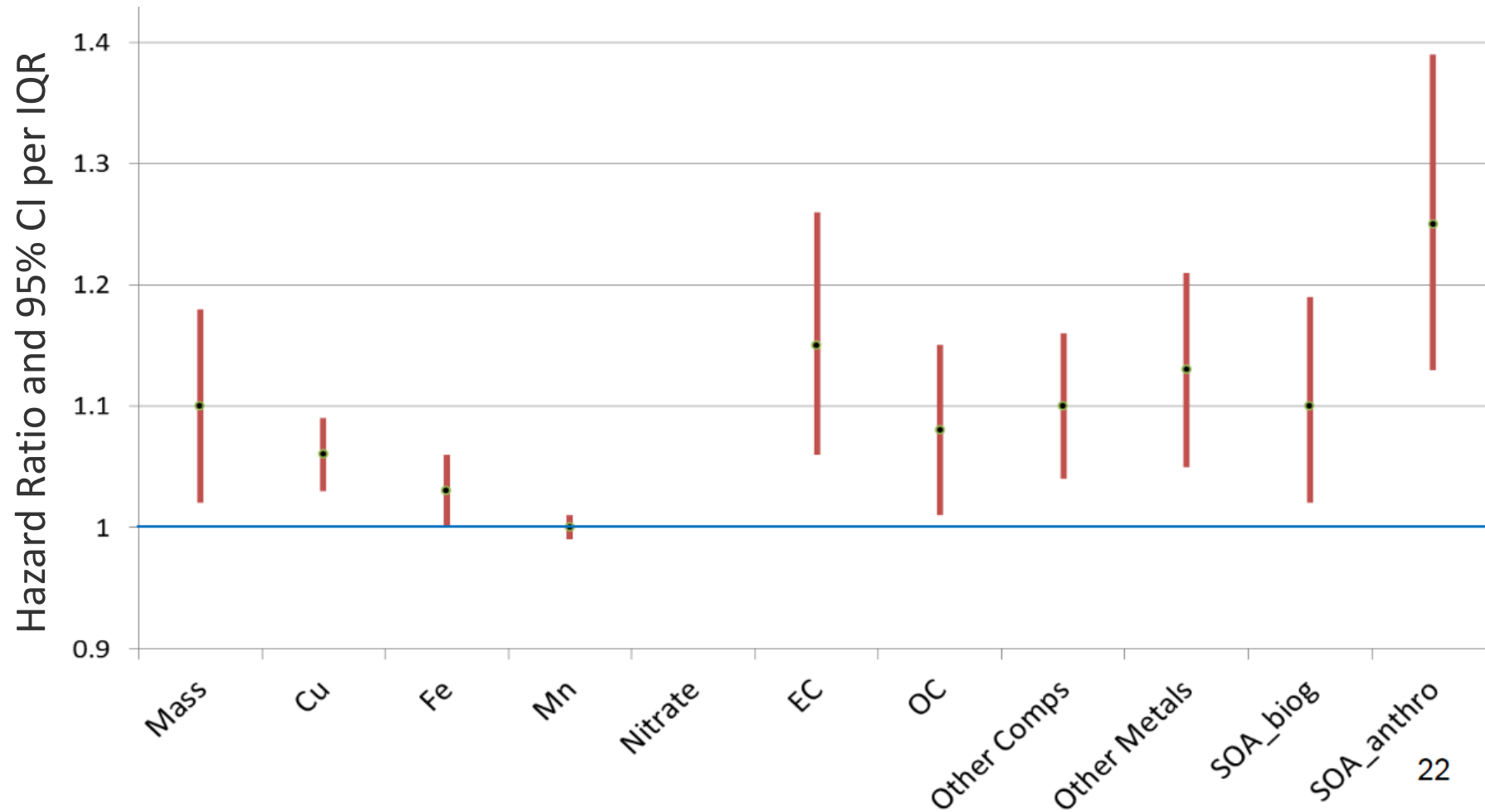
Follow-up for mortality for
2001-2007

100,000 California teachers
aged 30-80 years in 1995



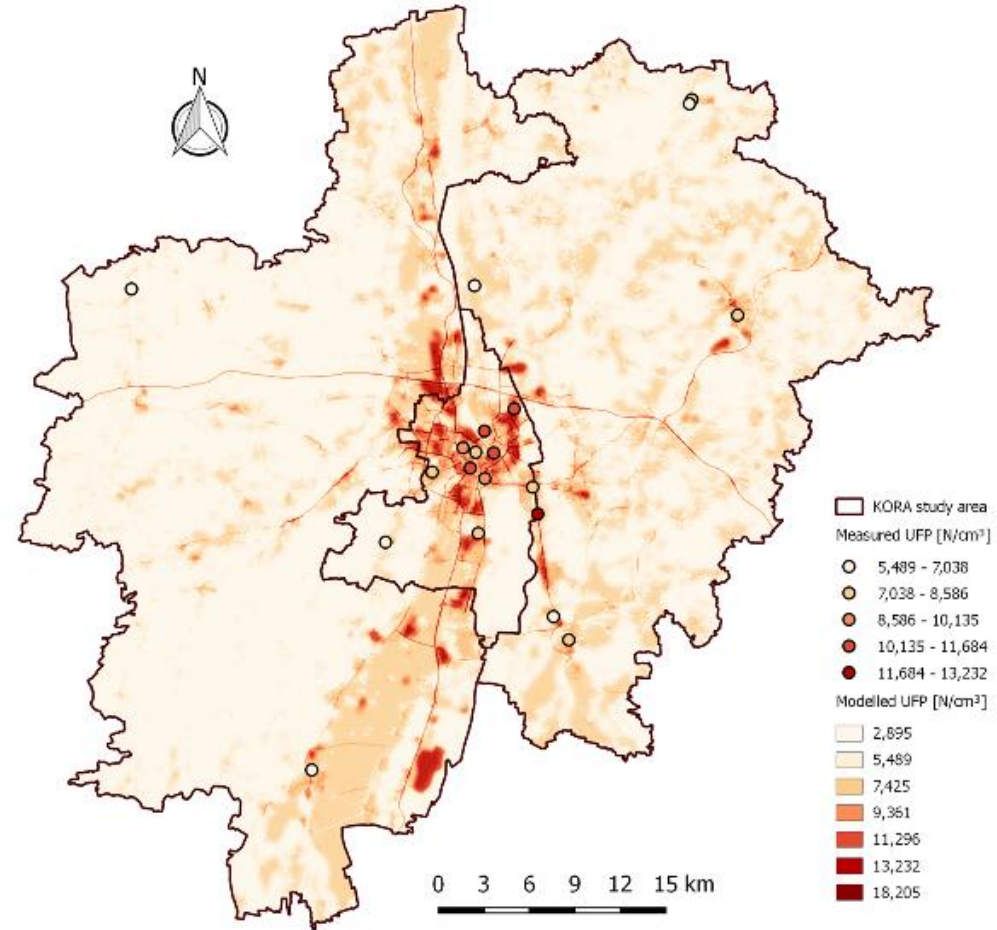
Ultrafine EC in Los Angeles and Counties ($\mu\text{g}/\text{m}^3$)

Ultrafine particles and Ischemic Heart Disease Mortality

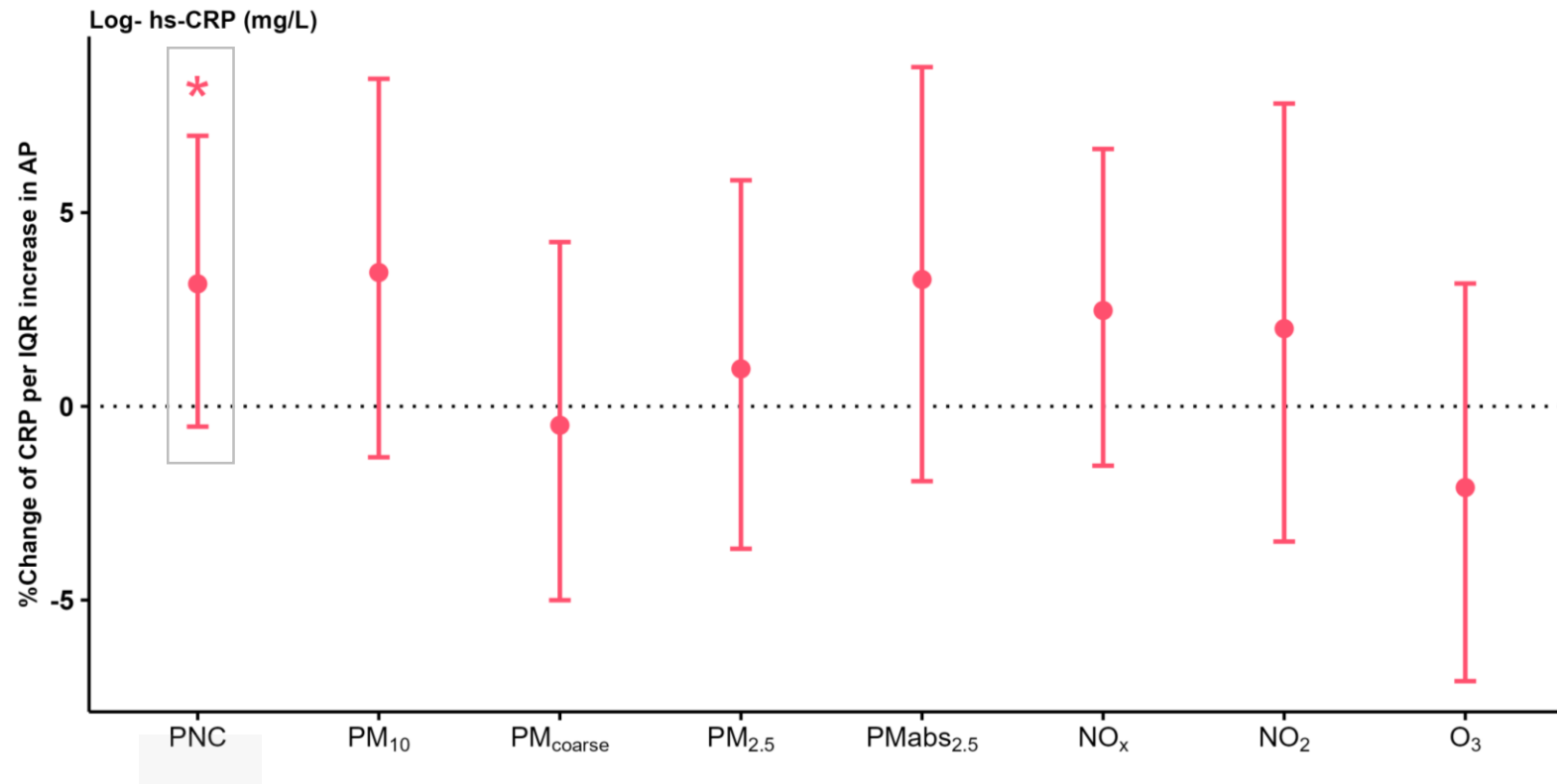


Land use regression-based modelling of ultrafine particles

Traffic load of major roads within 50m
% of industrial area within 300m
% of forest and seminatural areas, 100m
% of green area within 500m
Area of buildings within 25m

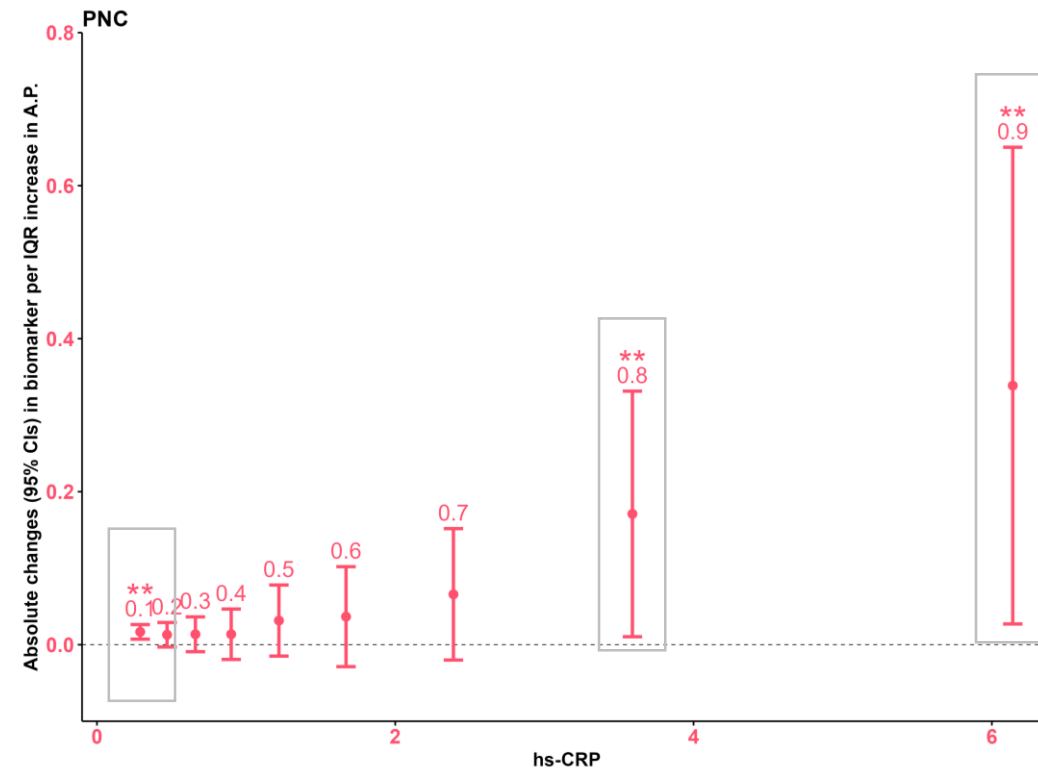


Ultrafine particles and inflammation



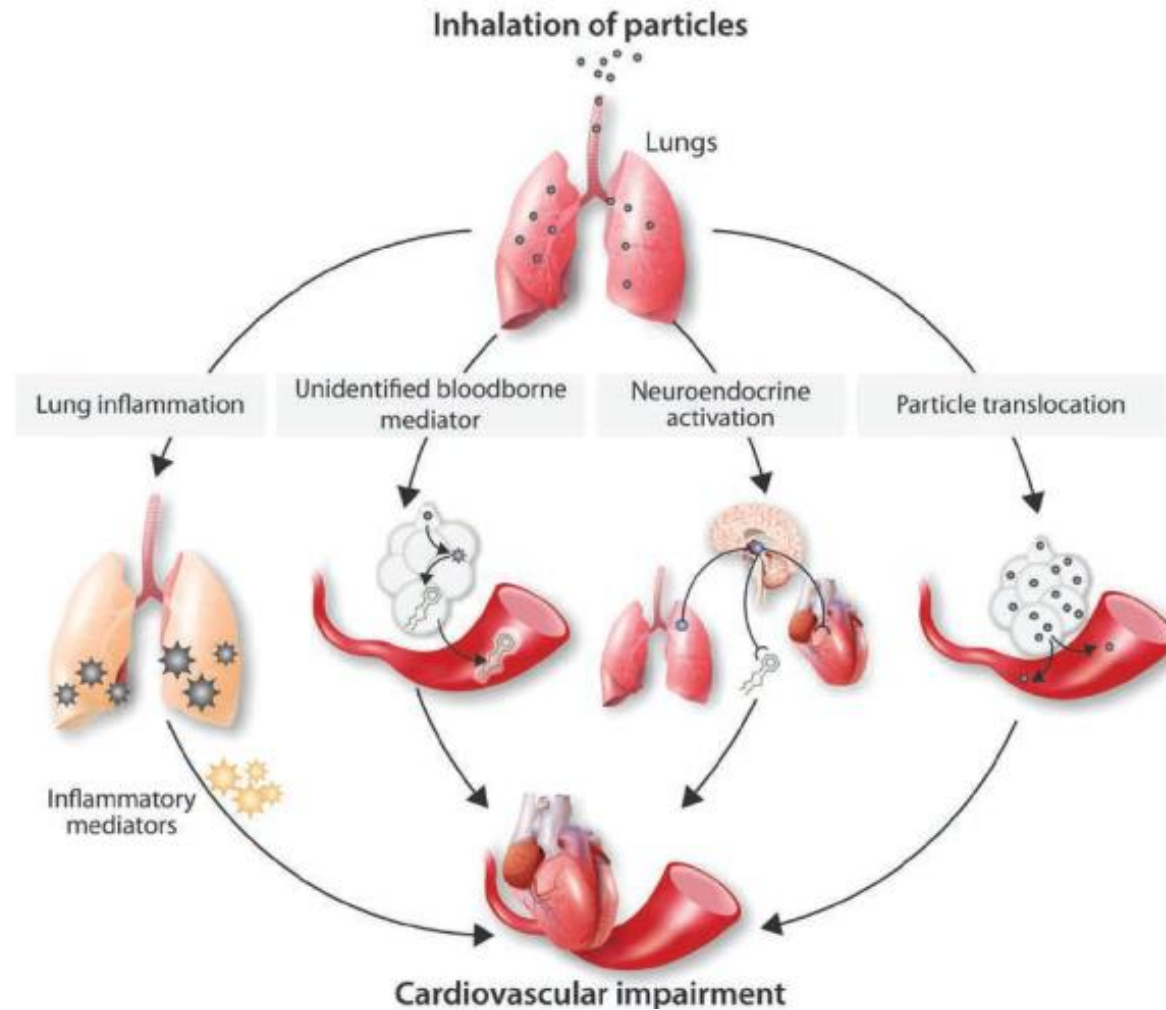
Ultrafine particles and inflammation: Quantile regression

Quantile regression analysis shows statistically significant positive associations at the **10th**, **80th**, **90th** percentiles.



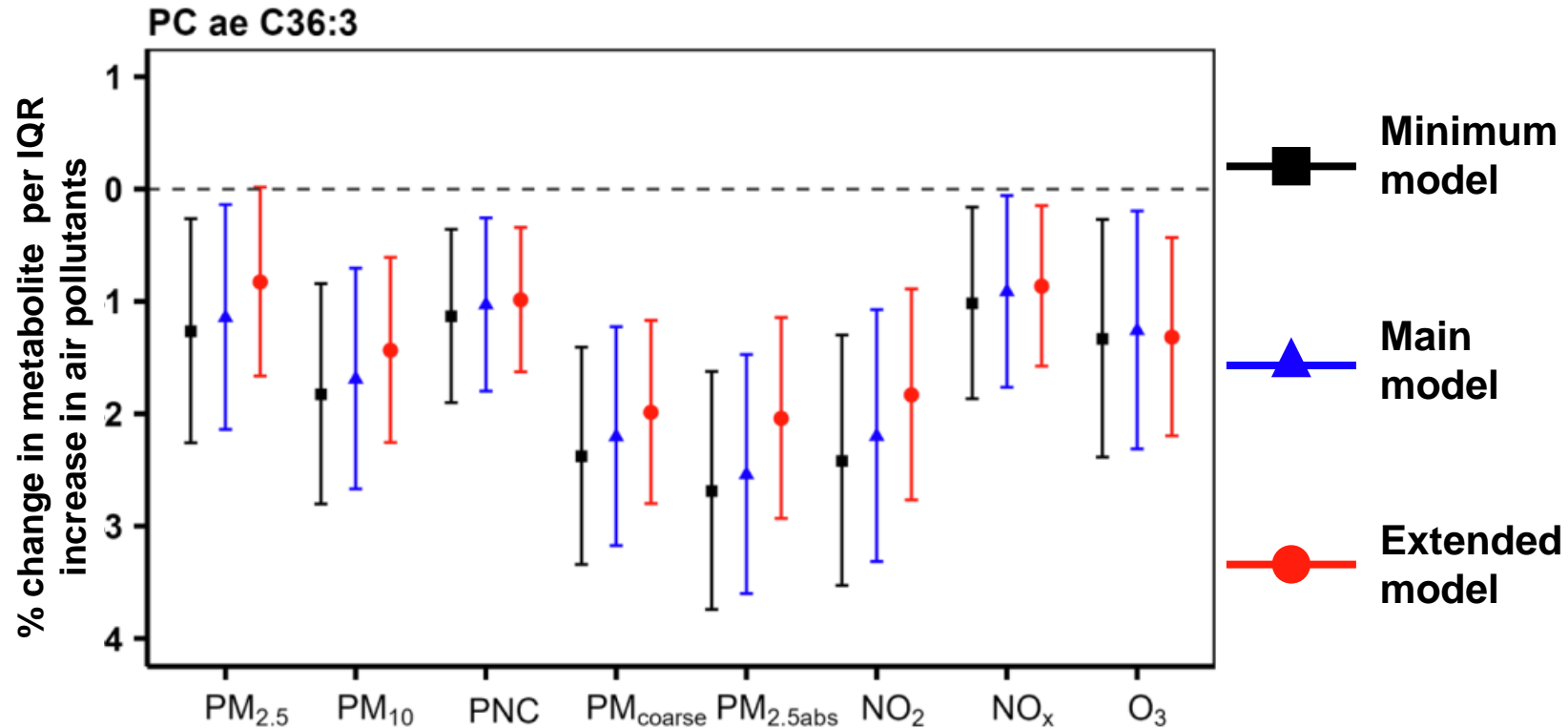
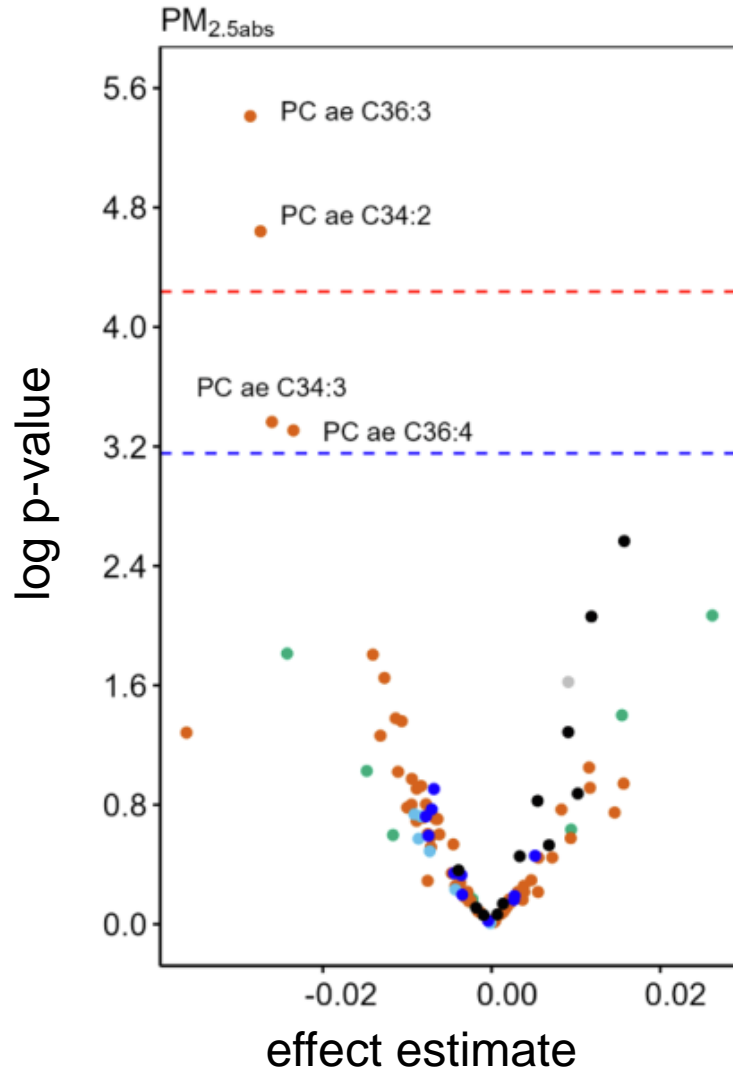
People with a **high level of CRP** show an **CRP response to UFP**.

Air pollution impacts cardiovascular disease



Miller & Newby 2020

Changes in metabolic signatures over 15 years



Linking molecular markers to incident myocardial infarction in two cohorts

Study

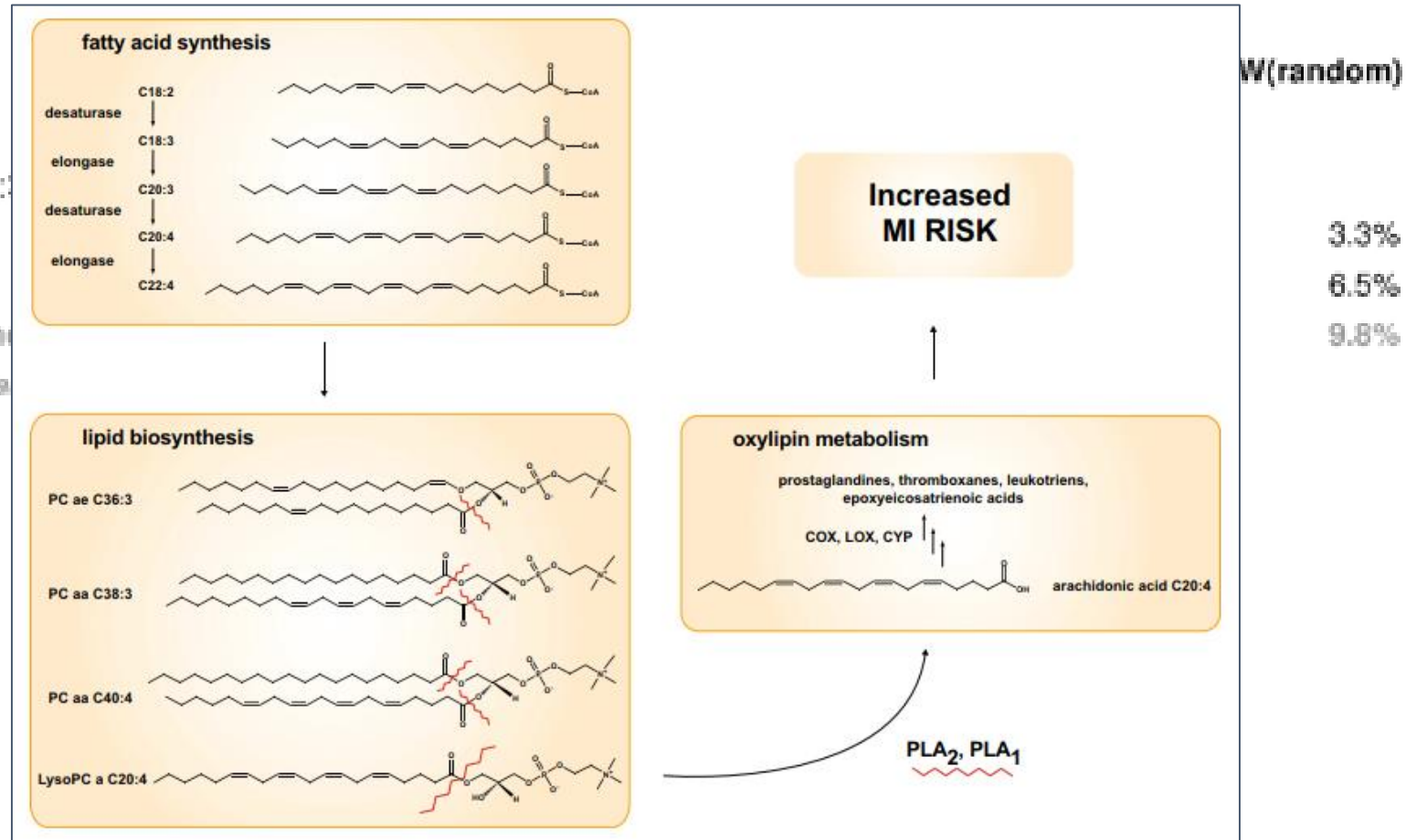
Acyl-alkyl-PC C38:3

Potsdam

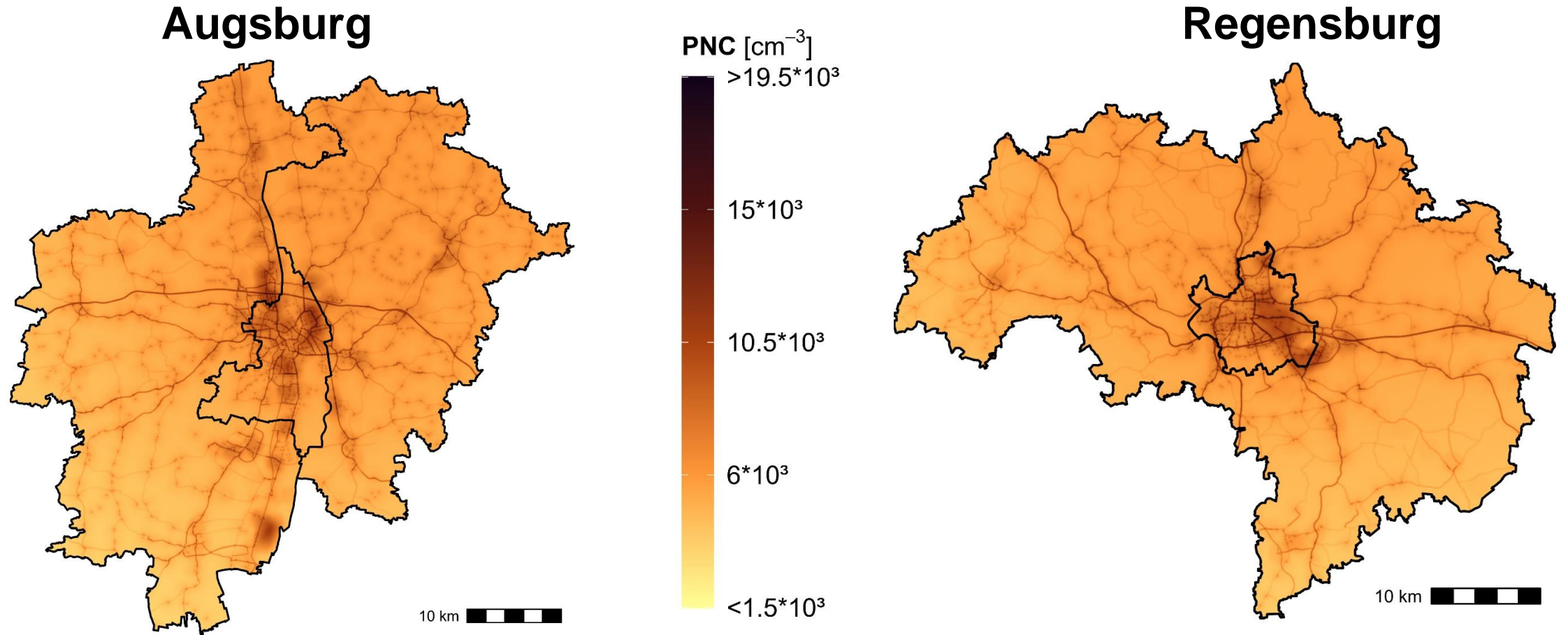
Heidelberg

Random effects meta-analysis

Heterogeneity: I-squared = 0%



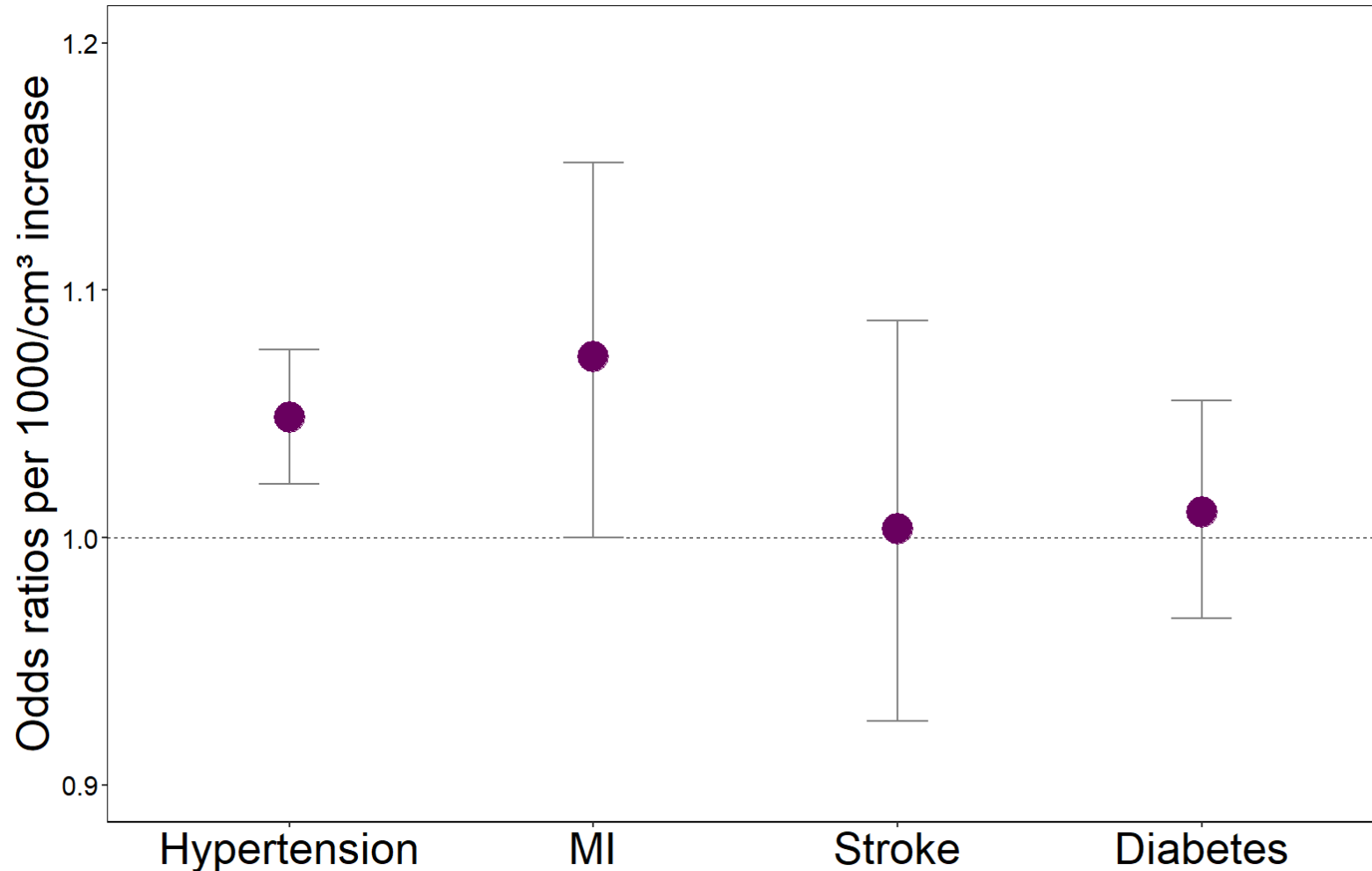
Estimated ultrafine number concentrations in regions of the German National Cohort (NAKO)



Wolf et al unpublished

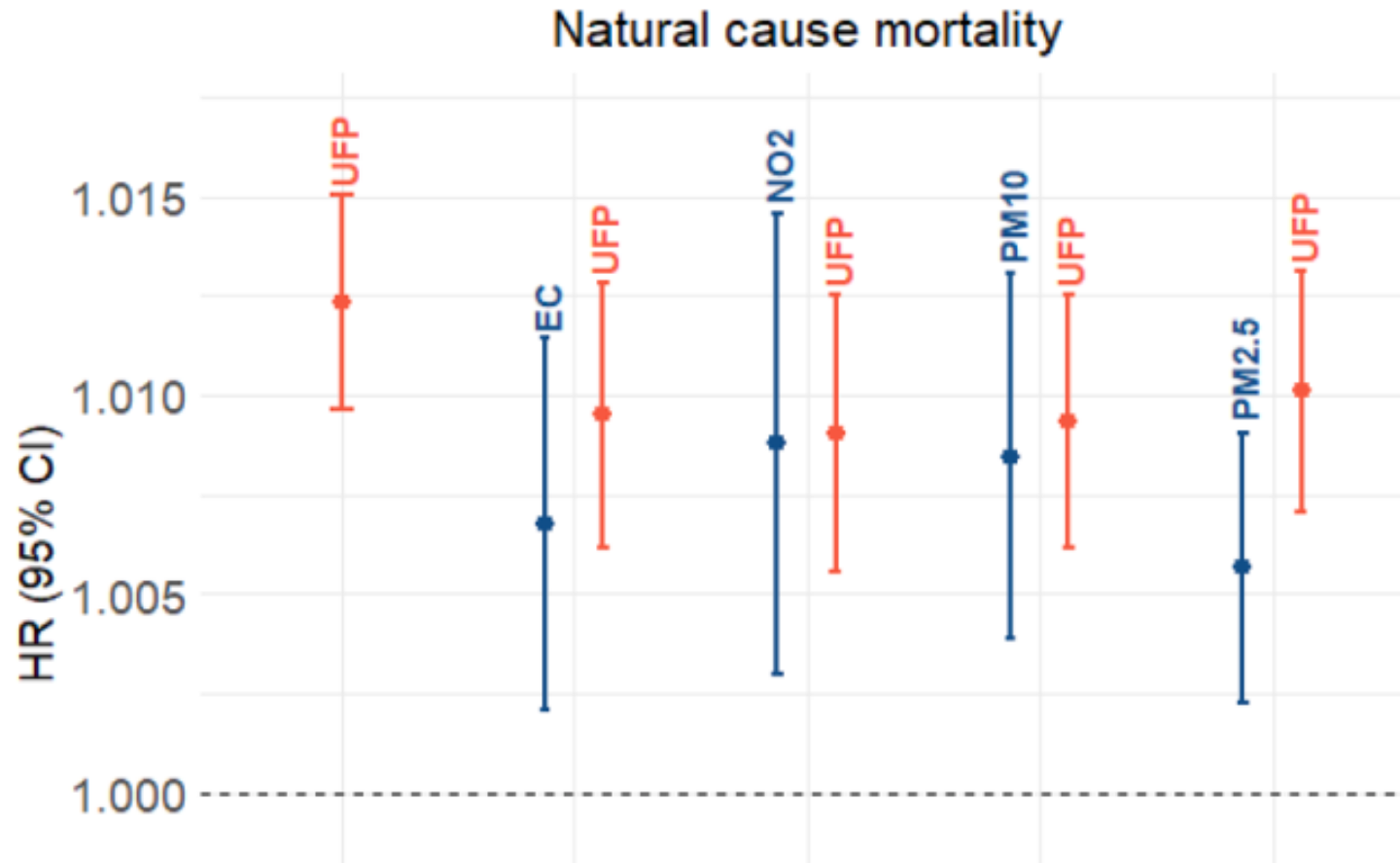


Ultrafine particles and cardiometabolic diseases

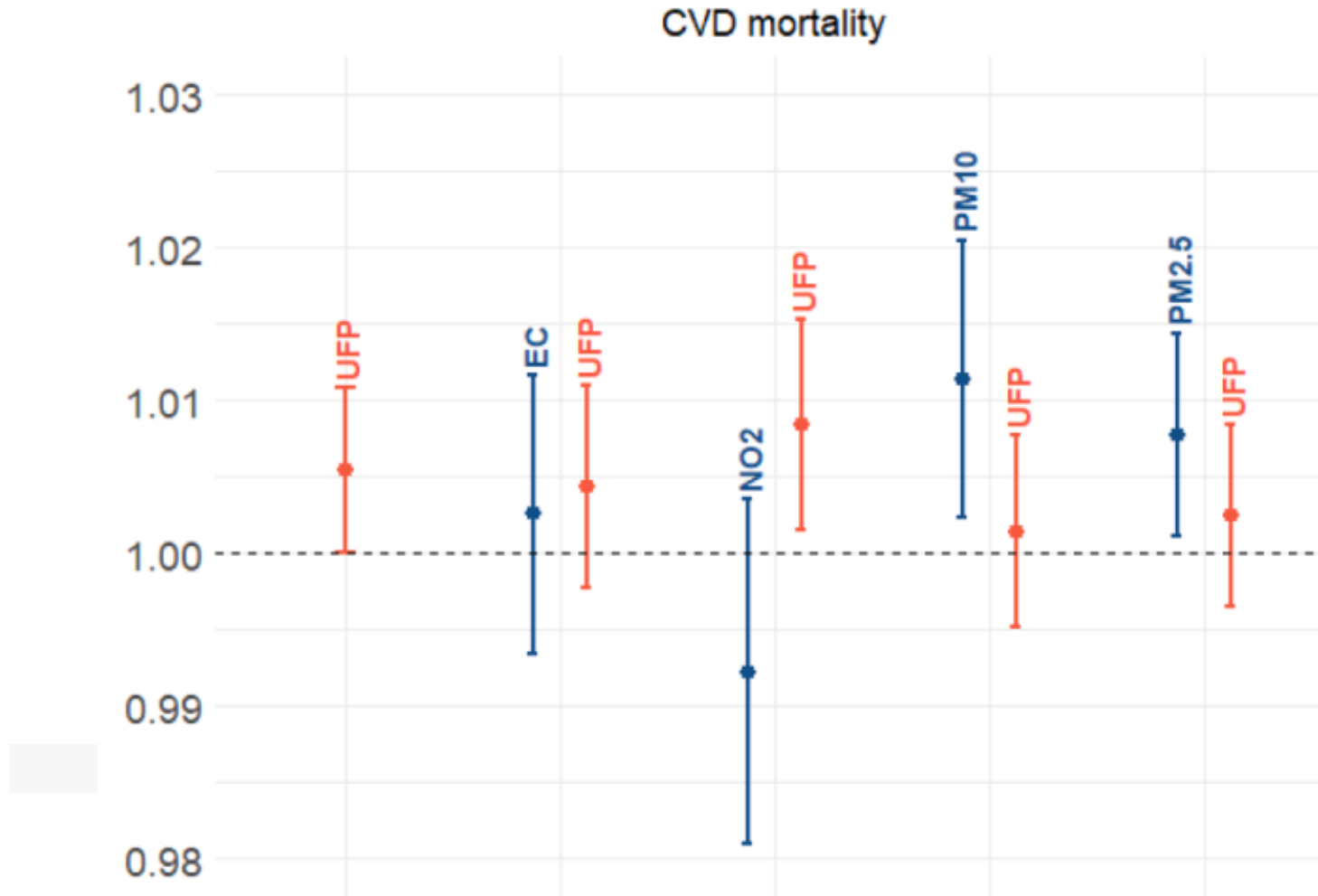


- Risk for hypertension increases 5.0%
- Risk for prevalent myocardial infarction increases 7.4%
- No association between PNC and stroke or diabetes prevalence

Particle number concentrations and mortality



Particle number concentrations and mortality

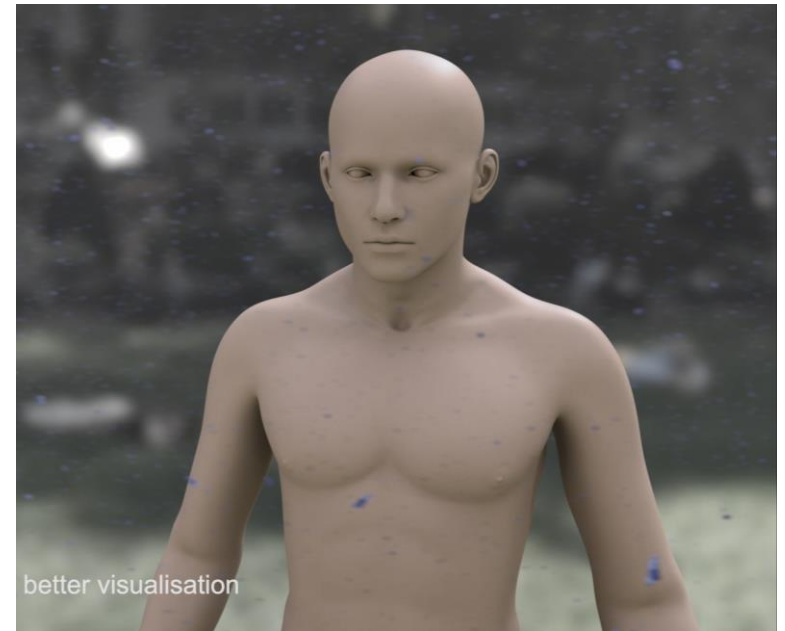


Bouma et al. EI 2023

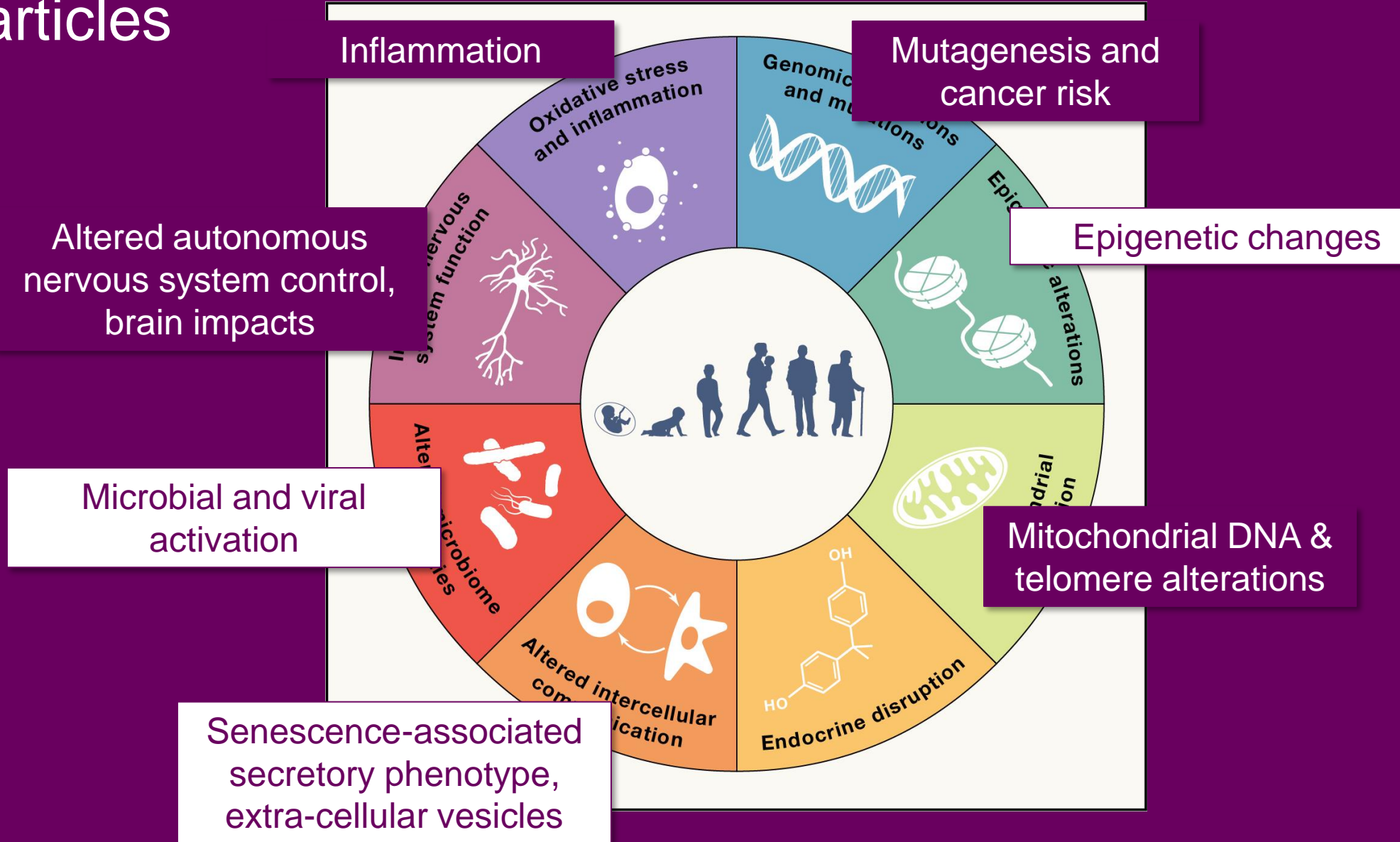
⇒ Reducing ultrafine particles is an important future task

Summary on Ultrafine Particles

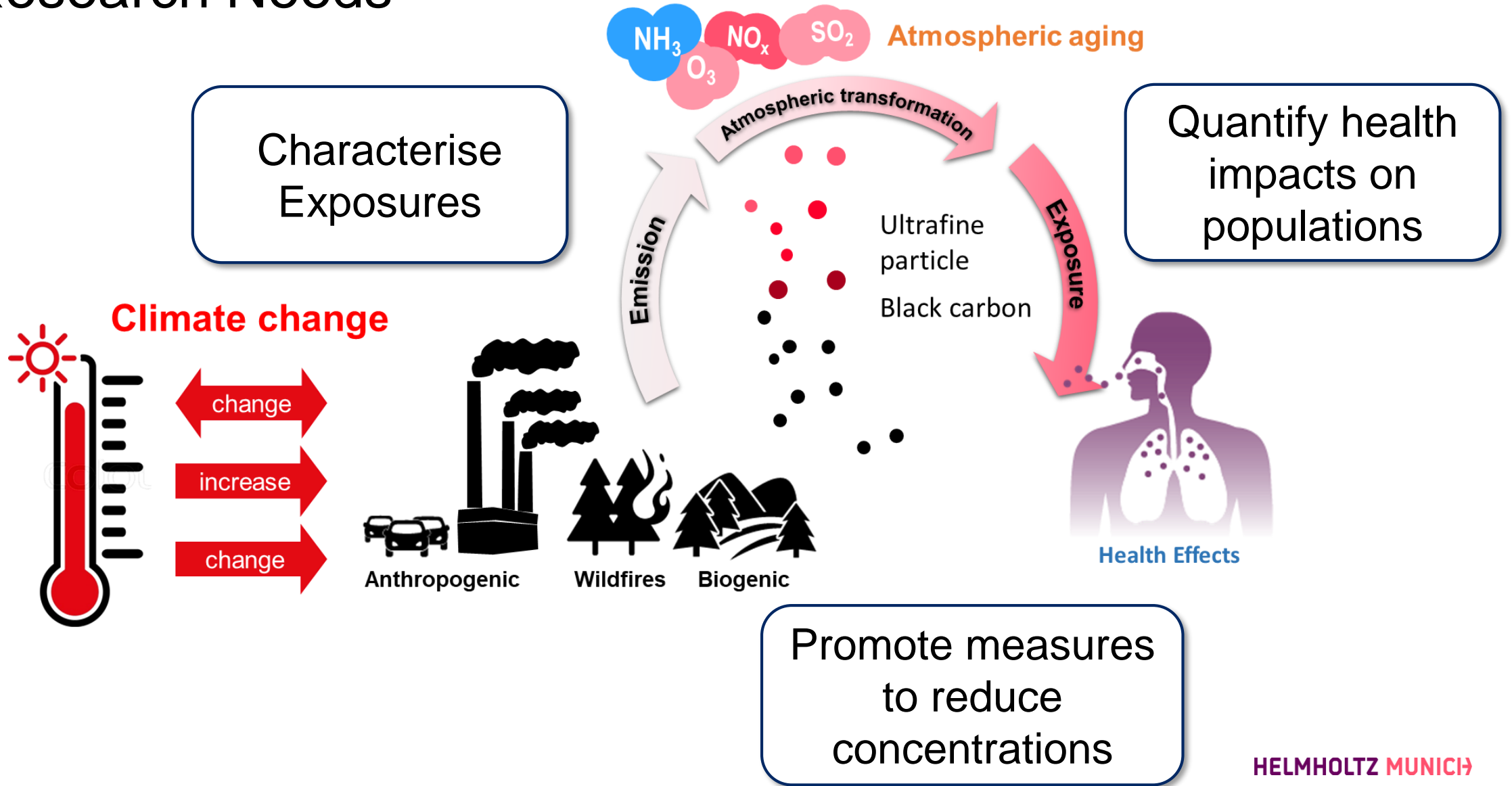
- Exposures to ultrafine and fine particles differ in space and time
- Experimental and epidemiological studies suggest independent short-term health effects
- Studies on long-term health effects are emerging



Ultrafine particles & Health



Research Needs



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Thank you.