Long-term exposure to ultrafine particles and incidence of cardiovascular and cerebrovascular disease in the EPIC-NL cohort

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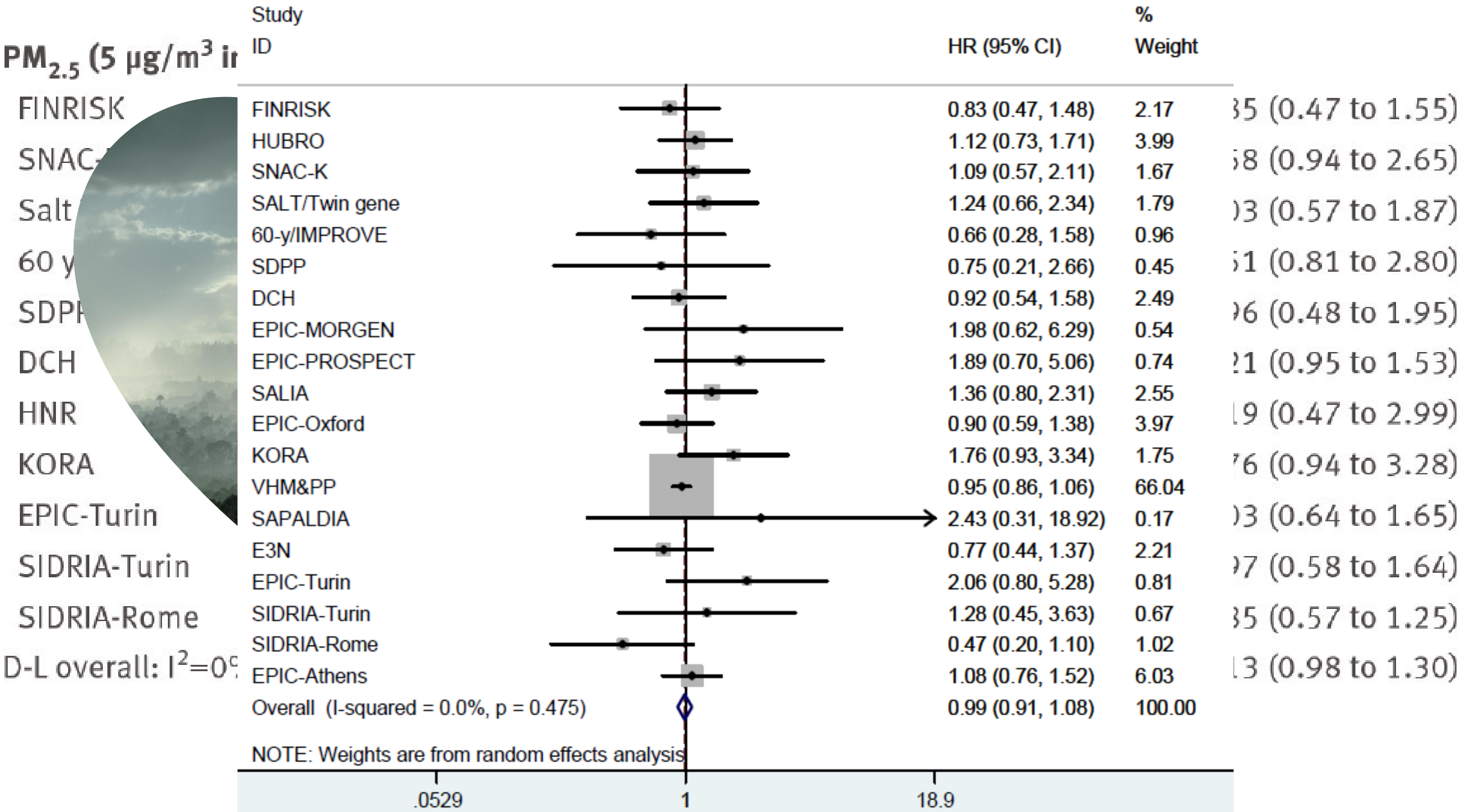
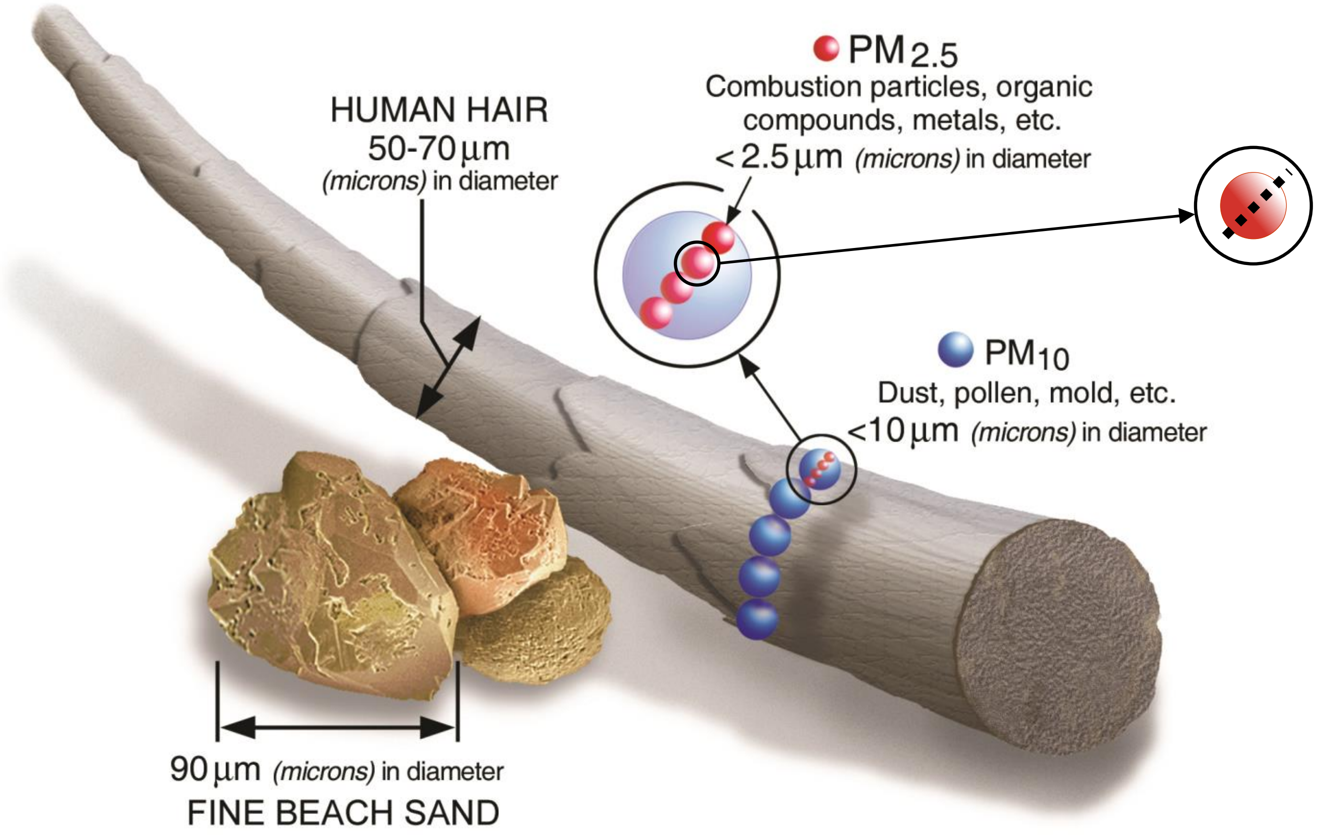
Air pollution & CVD



CesaroniG,ForastiereF,StafoggiaM,AndersenZJ,BadaloniC,BeelenR,etal. 2014.Longtermexposuretoambientairpollutionandincidenceofacutecoro- naryevents:prospectivecohortstudyandmeta-analysisin11Europeancohorts fromtheESCAPEproject.BMJ348:f7412,PMID: 24452269, https://doi.org/10. 1136/bmj.f7412.

Beelen R, Stafoggia M, Raaschou-Nielsen O, Andersen ZJ, Xun WW, Katsouyanni K, et al. 2014. Long-term exposure to air pollution and cardiovascular mortality: an analysisof22Europeancohorts.Epidemiology25(3):PMID: 24589872,https://doi.org/10.1097/EDE.0000000000000076.

UFPs



- UFP
- <100nm
- High surface area to mass ratio
- May not be reflected by conventional PM

Image modified from original, sourced from: EPA.gov

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UFPs & CVD

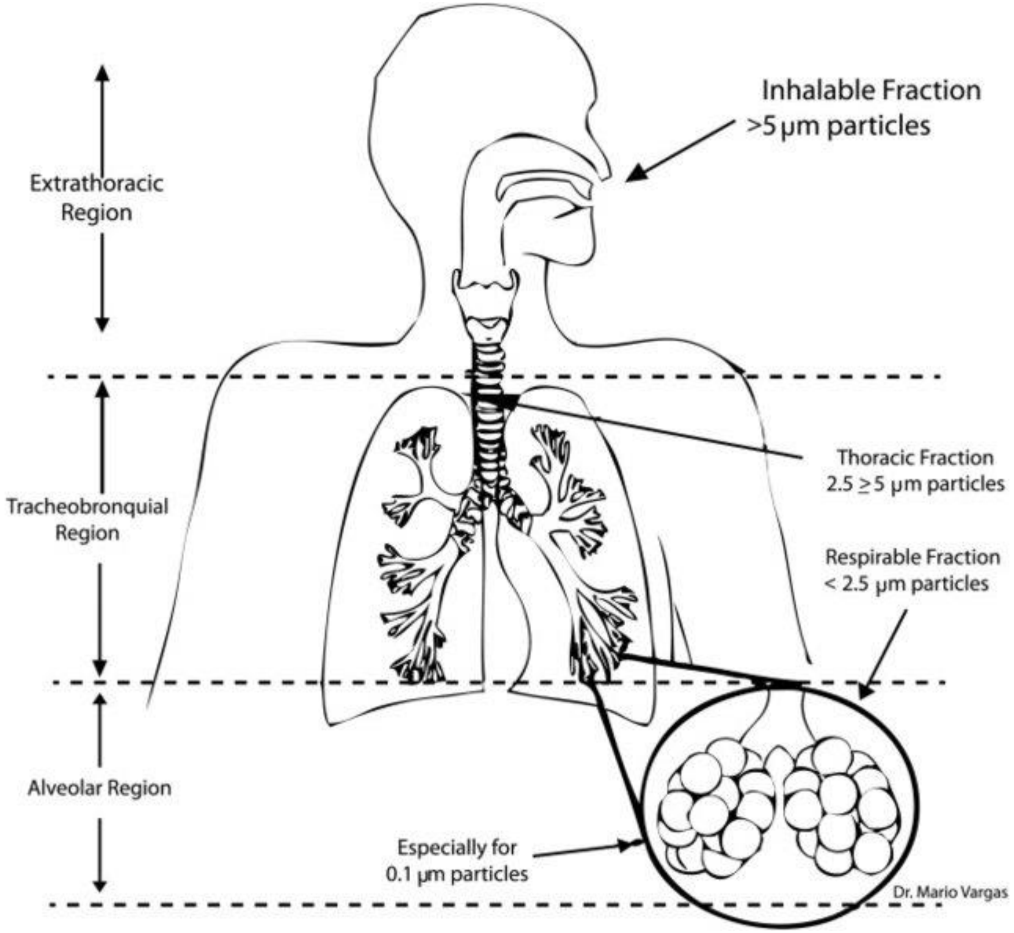
High alveolar deposition

Experimental & animal studies

- Biological plausibility

Some epi studies performed

- Short term effect
- Limited spatial scale
- Existing illness



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Project goals

Investigate the association between long-term UFP exposure & CVD

- EPIC-NL cohort
- High spatial scale

Compare to other pollutants

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Methods – study population

EPIC-NL

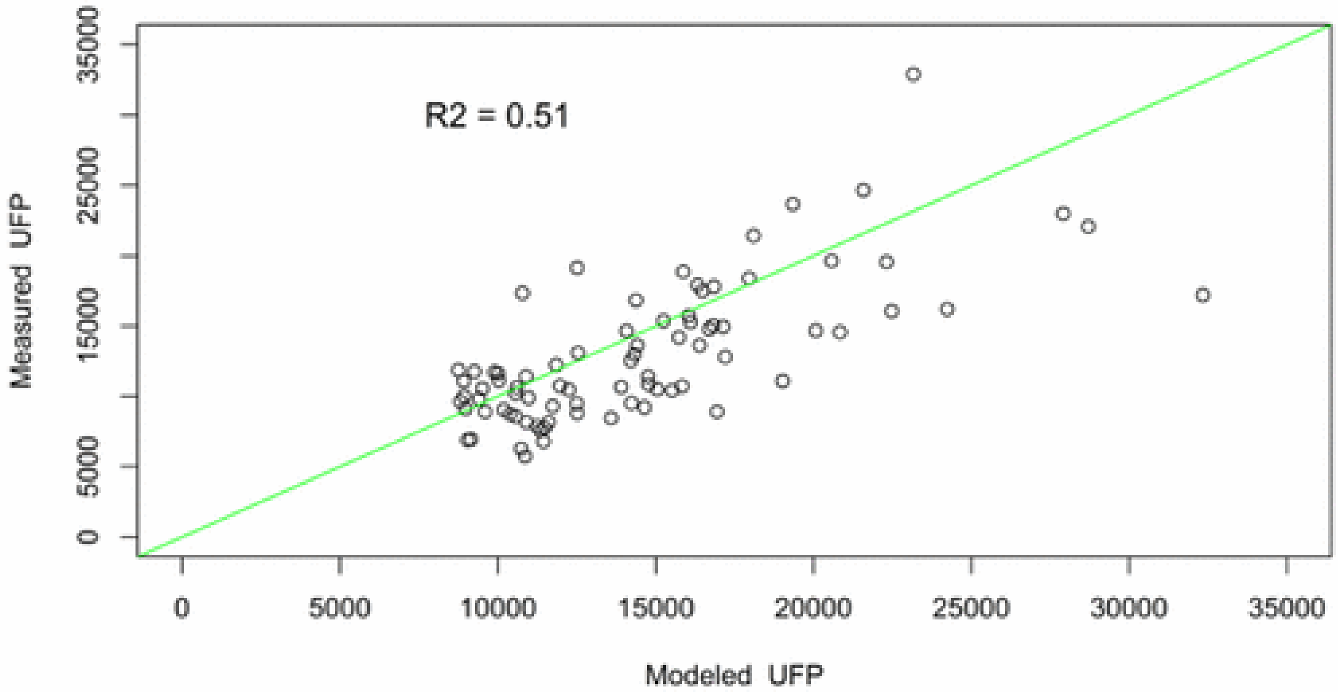
- Prospect
  - 17,357 women
  - 49 – 70 yrs
  - Enrolled from breast cancer screening program
- MORGEN
  - 23,100 men & women
  - 20 – 65 yrs
  - Population enrolment
- Recruitment 1993 – 1997

EPIC nl

Methods – UFP modelling

UFP predicted as per LUR models by van Nunen et.al.

- 6 European countries
- 242 monitoring sites (NL)
- 3 x 30 minutes per site
- LUR models developed
  - Traffic/industry etc.
  - R^2 = 51%



van NunenE,VermeulenR,TsaiMY,Probst-HenschN,IneichenA,DaveyM,etal. 2017. LanduseregressionmodelsforultrafineparticlesinsixEuropeanareas. Environ SciTechnol51(6):3336–3345. PMID: 28244744, https://doi.org/10.1021/ acs.est.6b05920

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Methods – other pollutants

LUR models developed for ESCAPE project

- 40 (PM) to 80 (NO) sites
- 3 x 14d period per site
- R^2 of LURs: 51% (PM_{coarse}) to 92% (BC)

- $PM_{2.5}$
- PM_{coarse}
- PM_{10}
- $PM_{2.5}$ absorbance (BC)
- NO_x
- NO_2

Beelen R,HoekG,VienneauD,EeftensM,DimakopoulouK,PedeliX,etal.2013. DevelopmentofNO2andNOxlanduseregressionmodelsforestimatingair pollutionexposurein36studyareasineurope – the ESCAPEproject.Atmos Environ 72:10–23, https://doi.org/10.1016/j.atmosenv.2013.02.037.

EeftensM,BeelenR,deHooghK,BellanderT,CesaroniG,CirachM,etal.2012. DevelopmentoflanduseregressionmodelsforPM(2.5),PM(2.5)absorbance, PM(10)andPM(coarse)in20Europeanstudyareas;resultsoftheESCAPEpro- ject.EnvironSciTechnol46(20):11195–11205,PMID: 22963366, https://doi.org/10. 1021/es301948k.

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Outcomes – incident disease

Endpoints	N. events	ICD9	ICD10
All cardiovascular disease	4,304	410-414, 427.5, 428, 415.1, 443.9, 430-438, 440-442, 444, 798.1,798.2, 798.9	I20-I26, I46, R96, G45, I60-I67, I69, I70-I74, I50
Coronary heart disease	2,399	410-414	I20-I25
Acute myocardial infarction	797	410	I21, I22
Heart failure	369	428	I50
Cerebrovascular event	1,283	430-438	I60-I67, I69, G45
Ischemic CVA (including TIA)	846	433-435	I63, I65, G45
Haemorrhagic CVA	241	430, 431, 432	I60-I62

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Methods – Cox models

Cox proportional hazards

- Age as time scale

One & two pollutant models

- Pollutants predicted at baseline address

Models adjusted for:

- Sex
- Year of enrolment
- Smoking status, intensity, and duration
- Fruit and vegetable intake
- BMI
- Education
- Marital status
- Area-level SES

Sensitivity tests of model robustness

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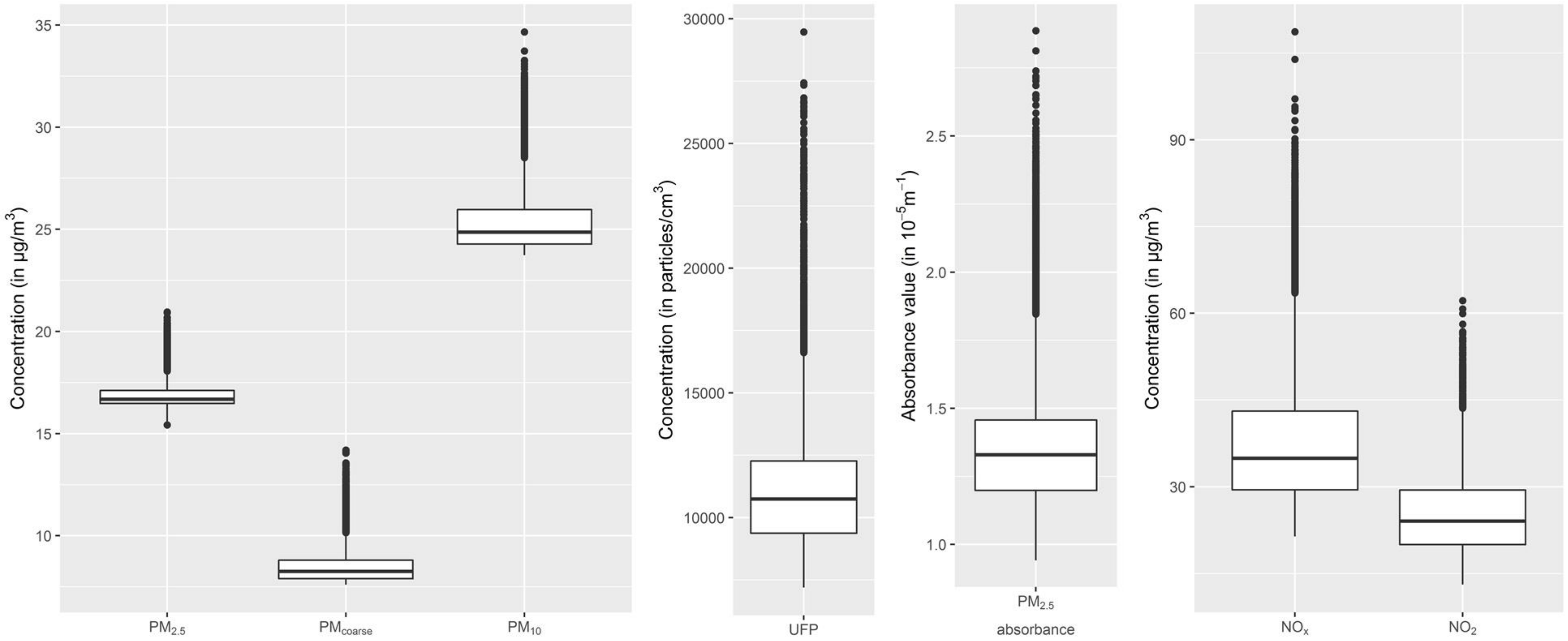
Results – population overview

Characteristic	N (%), or mean ± SD (min - max)
No. of participants	33,831
Age at baseline	50 ± 11
Years of follow-up	15 ± 2.4
Gender	
Male	7,846 (23)
Female	25,985 (77)
Smoking status	
Current	10,025 (30)
Former	10,837 (32)
Never	12,832 (38)

Characteristic	N (%), or mean ± SD (min - max)
Marital Status	
Single	4,789 (14)
Married/with partner	24,328 (72)
Divorced/separated	2,646 (8)
Widowed	1,892 (6)
Education level	
Primary school	5,678 (17)
Secondary school	21,426 (64)
University	6,508 (19)

Results – pollutants



Results – internal correlation

UFP	0.54	0.74	0.82	0.83	0.74	0.80
	$PM_{2.5}$	0.31	0.50	0.75	0.44	0.26
		PM_{coarse}	0.83	0.67	0.75	0.78
			PM_{10}	0.89	0.86	0.84
				BC	0.82	0.77
					NO_x	0.85
						NO_2

Results - CVD

HRs for the following increments: 10,000 particles/cm_3 for UFP, 5 µg/m^3 for $PM_{2.5}$, 5 µg/m^3 for PM_{coarse}, 10 µg/m^3 for PM_{10},, $1\times10^{-5}m^{-1}$ for BC, 20 µg/m^3 for NO_x, and 10 µg/m^3 for NO_2.

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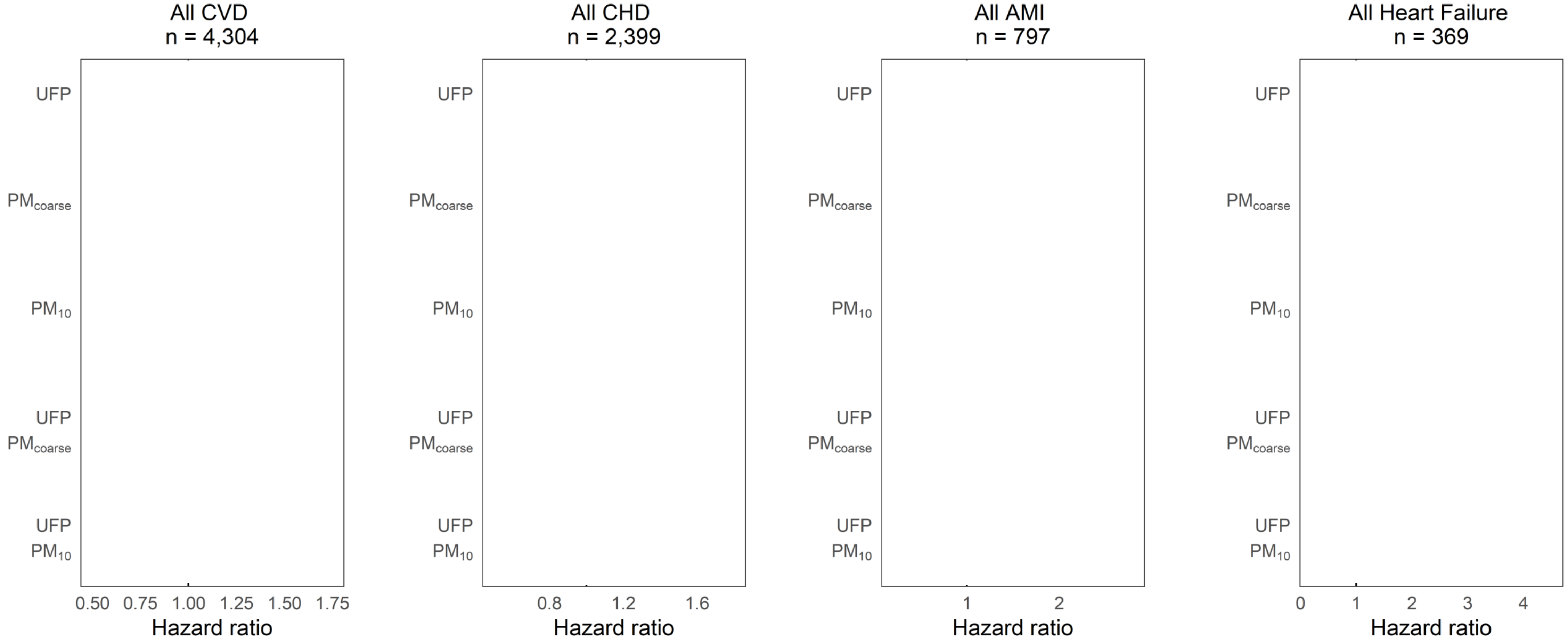
Selected Bipollutant models - CVD



HRs for the following increments: 10,000 particles/cm_3 for UFP, 5 μg/m^3 for $PM_{2.5}$, 5 μg/m^3 for PM_{coarse}, 10 μg/m^3 for PM_{10},, 1×$10^{-5}$$m^{-1}$ for BC, 20 μg/m^3 for NO_x, and 10 μg/m^3 for NO_2.

Results - CVA

HRs for the following increments: 10,000 particles/cm_3 for UFP, 5 µg/m^3 for $PM_{2.5}$, 5 µg/m^3 for PM_{coarse}, 10 µg/m^3 for PM_{10},, $1 \times 10^{-5} m^{-1}$ for BC, 20 µg/m^3 for NO_x, and 10 µg/m^3 for NO_2.

Sensitivity analysis

Findings generally robust across multiple sensitivity tests

- Residential stability
- Urban/rural separation
- Complete confounder information

Limitations

Temporal application of LUR models

- UFP measured in 2017
- Only one prediction per person
- Recruitment for EPIC began in 1990s

Exposure misclassification

- R^2 for UFP: 50%

Collinearity of measurements

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Summary

CVD risk may not be adequately/completely explained by larger PM fractions

UFP gives additional insight into CVD risk

Issues relating to model performance and temporal application need further assessment.

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