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Long-term exposure to ultrafine particles and lung cancer mortality and incidence

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Long-term exposure to ultrafine particles and natural and cause-specific mortality

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ABSTRACT

Background: Health implications of long-term exposure to ubiquitously present ultrafine particles (UFP) are uncertain. The aim of this study was to investigate the associations between long-term UFP exposure and natural and cause-specific mortality (including cardiovascular disease (CVD), respiratory disease, and lung cancer) in the Netherlands.

Methods: A Dutch national cohort of 10.8 million adults aged ≥ 30 years was followed from 2013 until 2019. Annual average UFP concentrations were estimated at the home address at baseline, using land-use regression models based on a nationwide mobile monitoring campaign performed at the midpoint of the follow-up period. Cox proportional hazard models were applied, adjusting for individual and area-level socio-economic status covariates. Two-pollutant models with the major regulated pollutants nitrogen dioxide (NO_2) and fine particles ($PM_{2.5}$ and PM_{10}), and the health relevant combustion aerosol pollutant (elemental carbon (EC)) were assessed based on dispersion modelling.

Results: A total of 945,615 natural deaths occurred during 71,008,209 person-years of follow-up. The correlation of UFP concentration with other pollutants ranged from moderate (0.59 ($PM_{2.5}$)) to high (0.81 (NO_2)). We found a significant association between annual average UFP exposure and natural mortality [HR 1.012 (95 % CI 1.010–1.015), per interquartile range (IQR) (2723 particles/cm^3) increment]. Associations were stronger for respiratory disease mortality [HR 1.022 (1.013–1.032)] and lung cancer mortality [HR 1.038 (1.028–1.048)] and weaker for CVD mortality [HR 1.005 (1.000–1.011)]. The associations of UFP with natural and lung cancer mortality attenuated but remained significant in all two-pollutant models, whereas the associations with CVD and respiratory mortality attenuated to the null.

Conclusion: Long-term UFP exposure was associated with natural and lung cancer mortality among adults independently from other regulated air pollutants.

Health effects of long-term UFP exposure are largely unknown

- Widespread exposure from combustion sources
- Toxicological evidence for harmful effects
- Under-researched due to difficulties of exposure assessment
- Not routinely measured and poorly represented by conventional mass-based measurements of particulate matter -> unregulated
- USEPA & Dutch Health Council -> evidence is “insufficient”

Previous research

A Section 508–conformant HTML version of this article is available at http://dx.doi.org/10.1289/ehp.1408565.

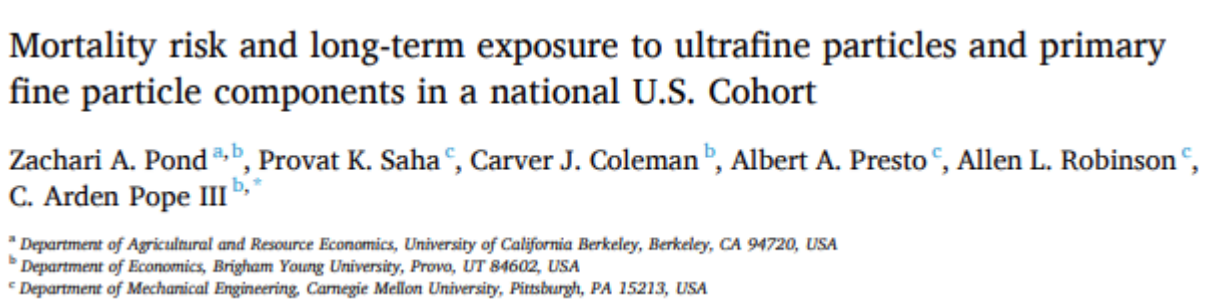
Research

Associations of Mortality with Long-Term Exposures to Fine and Ultrafine Particles, Species and Sources: Results from the California Teachers Study Cohort

Bart Ostro,[1] Jianlin Hu,[2] Debbie Goldberg,[3] Peggy Reynolds,[3] Andrew Hertz,[3] Leslie Bernstein,[4] and Michael J. Kleeman[2]

[1]Air Pollution Epidemiology Section, California Office of Environmental Health Hazard Assessment, Oakland, California, USA; [2]Department of Civil and Environmental Engineering, University of California, Davis, Davis, California, USA; [3]Cancer Prevention Institute of California, Berkeley, Berkeley, California, USA; [4]City of Hope National Medical Center, Duarte, California, USA

- Association with ischemic heart disease mortality
- No association with all-cause and respiratory mortality



Mortality risk and long-term exposure to ultrafine particles and primary fine particle components in a national U.S. Cohort

Zachari A. Pond [a,b], Provat K. Saha [c], Carver J. Coleman [b], Albert A. Presto [c], Allen L. Robinson [c], C. Arden Pope III [b,*]

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- Associations with all-cause and cancer mortality
- Attenuation after adjustment for $PM_{2.5}$

Research question

Is there an association between long-term exposure to UFP and natural and cause-specific mortality?

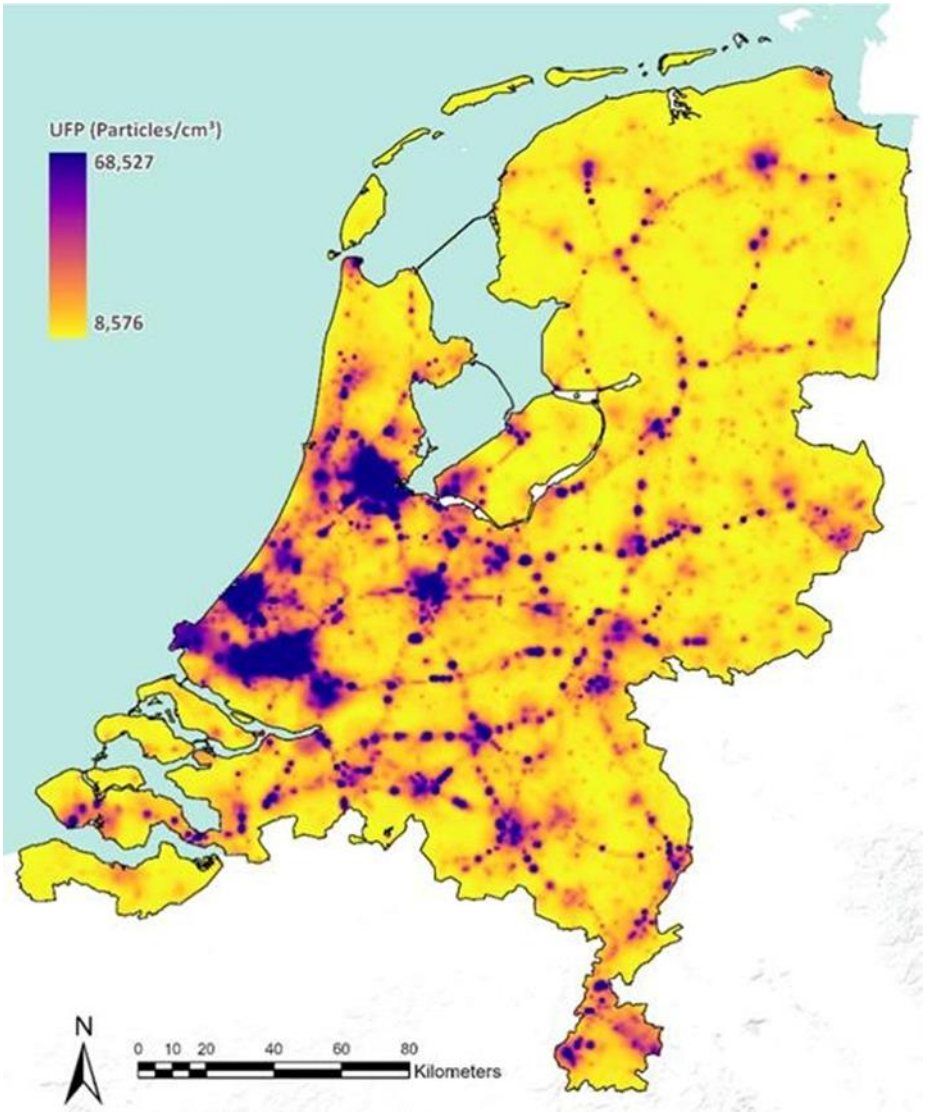
- **Lung cancer mortality**

Study population

- Administrative cohort: 10.8 million adults ≥30 years in the Netherlands
- Follow-up: 2013-2019
- Mortality outcomes:
  - Natural cause (ICD-10: A00-R99)
  - Lung cancer (C34)
  - Cardiovascular disease (I10-I70)
  - Non-malignant respiratory disease (J00-J99)

Exposure assessment

- Annual average UFP at residential address from nationwide LUR model based on mobile monitoring in 2016-2017
- Annual average NO_2, PM_{10}, $PM_{2.5}$, EC from dispersion models for 2016



(Kerckhoffs et al., 2021)

Data analysis

Cox proportional hazards models, age as timescale, stratified by sex, with 3 levels of adjustment:

1. No additional covariates
2. Individual covariates: household income, region of origin, marital status
3. Area-level covariates: mean income per income recipient, unemployment rate, social assistance, percentage non-western immigrants, and percentage of low education level on the neighborhood and regional level (main model)

Data analysis

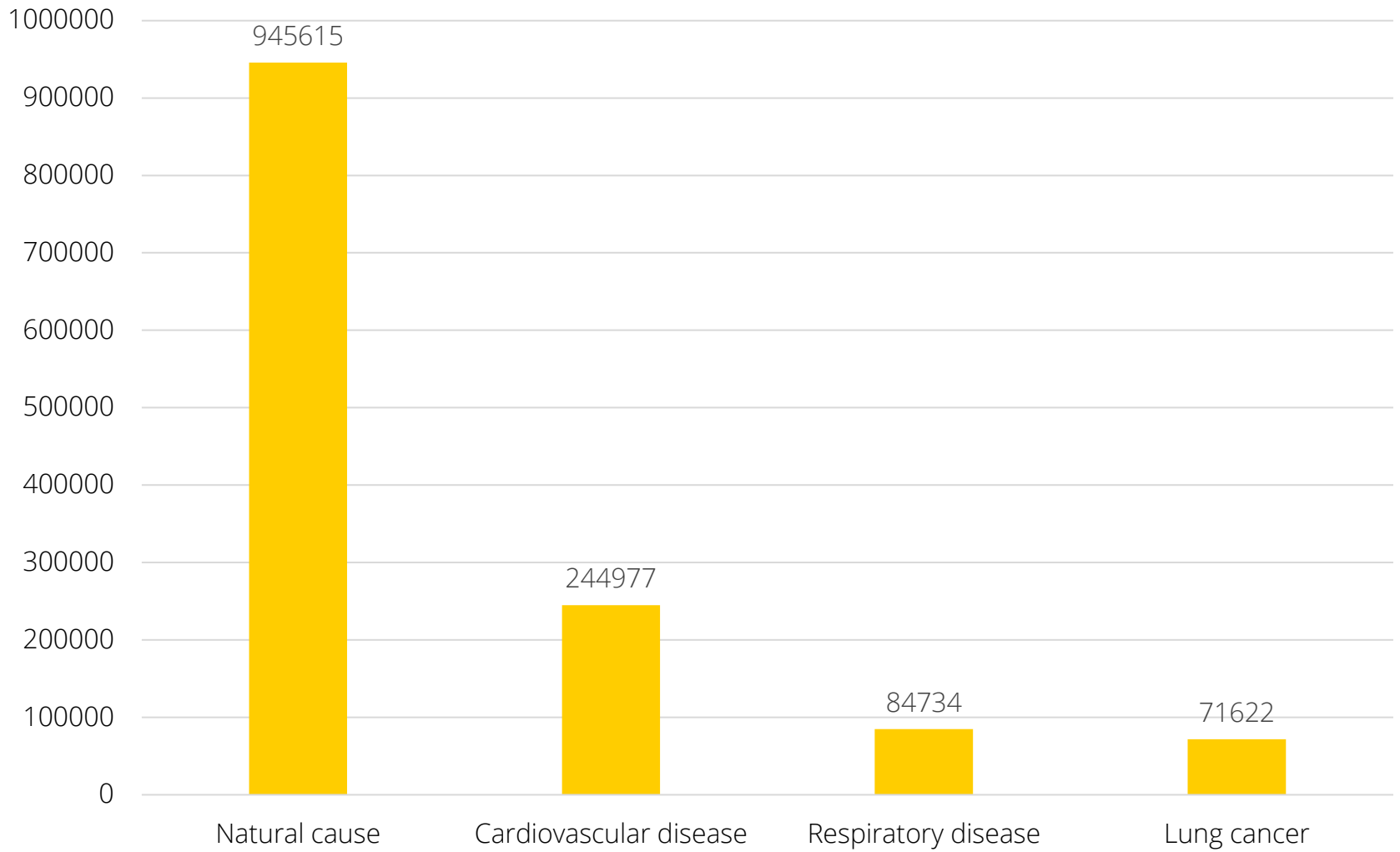
- Indirect adjustment for smoking and BMI using Public Health Monitor data
- Two-pollutant models: NO_2, PM_{10}, $PM_{2.5}$, EC
- Hazard ratio's per interquartile range increment of air pollution exposure

Results

Characteristics of the study population.

Covariate		
Individual covariates	**Category**	**N (%) or mean (sd)**
Age		54.3 (15.0)
Sex	Male	5,227,876 (48.7)
	Female	5,507,858 (51.3)
Marital status	Married	6,554,479 (61.1)
	Widowed	852,964 (7.9)
	Divorced	1,174,803 (10.9)
	Single	2,153,488 (20.1)
Region of origin	Dutch	8,732,131 (81.3)
	Western	1,055,828 (9.8)
	Other non-Western	319,633 (3.0)
	Suriname	200,271 (1.9)
	Turkey	197,419 (1.8)
	Morocco	163,338 (1.5)
	Antilles Netherlands	67,114 (0.6)
Standardized household income	<1 %	141,753 (1.3)
	1–5 %	192,802 (1.8)
	5–10 %	347,895 (3.2)
	10–25 %	1,306,536 (12.2)
	25–50 %	2,610,783 (24.3)
	50–75 %	2,920,752 (27.2)
	75–90 %	1,894,331 (17.6)
	90–95 %	657,075 (6.1)
	95–99 %	532,320 (5.0)
	>99 %	131,487 (1.2)
Area-level covariates	**Neighborhood (mean (sd))**	**Region (mean (sd))**
Percentage non-western immigrants	10.9 (13.5)	11.5 (7.5)
Social assistance (per 1000 inhabitants)	43.1 (44.1)	30.5 (2.5)
Unemployment (per 1000 inhabitants)	26.4 (9.6)	26.6 (3.6)
Mean income per income recipient (*€ 1000)	30.7 (6.9)	46.6 (16.5)
Percentage low education	32.0 (10.3)	31.9 (3.1)

Mortality cases during follow-up



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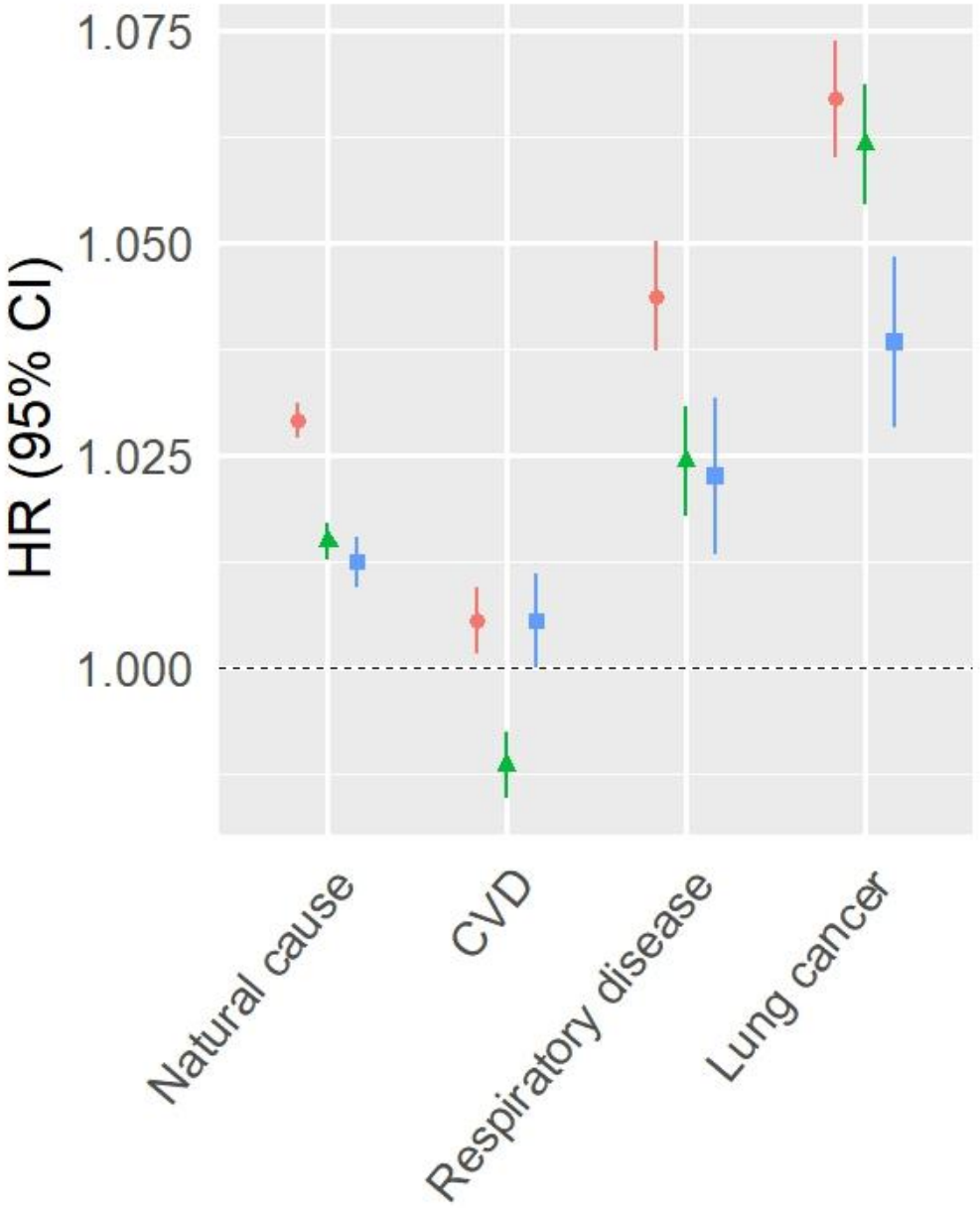
Air pollution exposure

	Median	Inter-quartile range
UFP (particles/cm^3)	**10805**	**2723**
NO_2 (µg/m^3)	19.5	6.52
PM_{10} (µg/m^3)	18.32	2.06
$PM_{2.5}$ (µg/m^3)	11.26	1.47
EC (µg/m^3)	0.82	0.24

Correlations between pollutants

	UFP	NO_2	PM_{10}	$PM_{2.5}$	EC
UFP	1				
NO_2	0.81	1			
PM_{10}	0.70	0.86	1		
$PM_{2.5}$	0.59	0.81	0.92	1	
EC	0.75	0.93	0.87	0.90	1

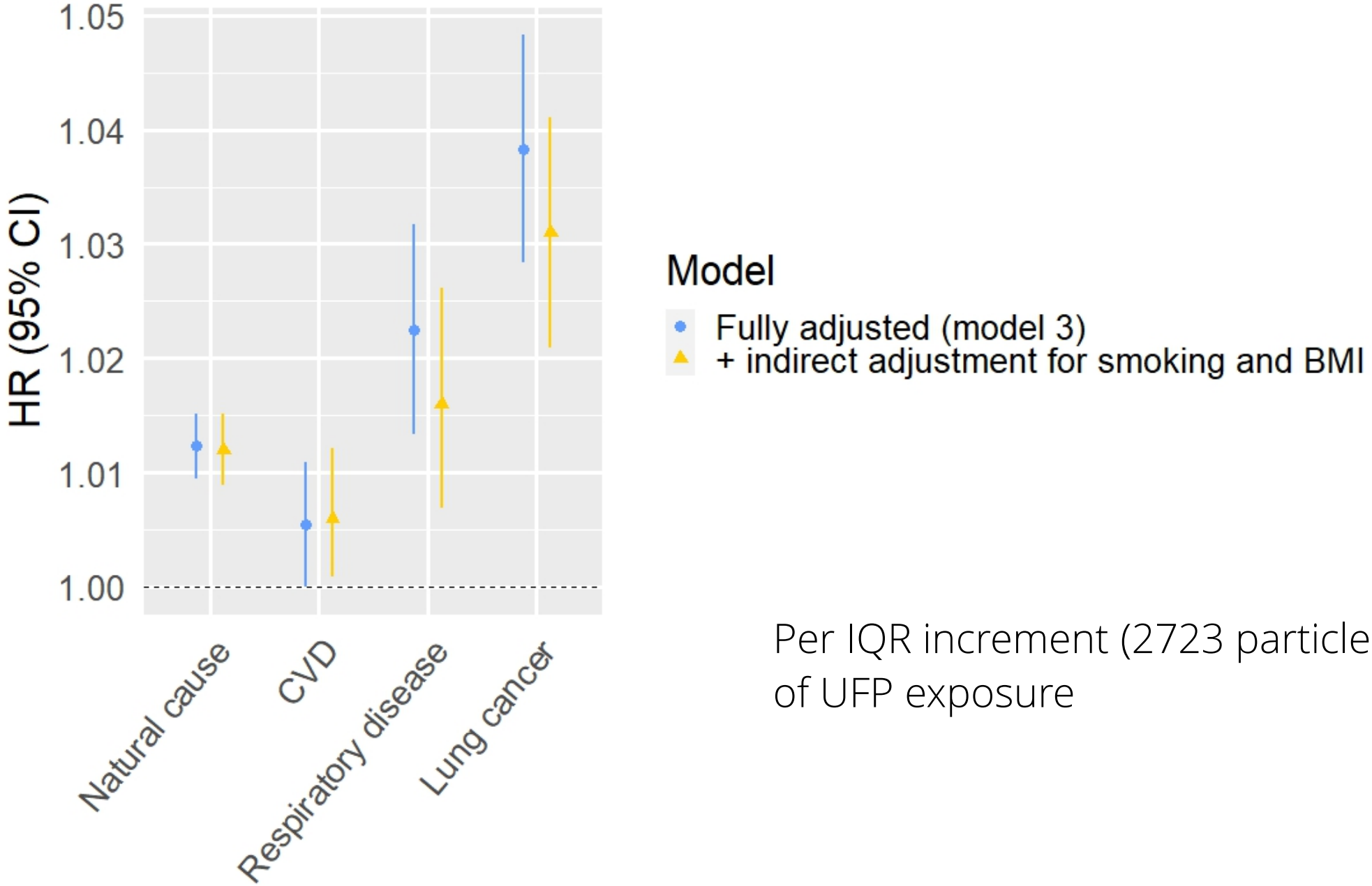
Associations of UFP and mortality



Model
- Unadjusted (model 1)
- Adjusted for individual-level covariates (model 2)
- Fully adjusted (model 3)

Per IQR increment (2723 particles/cm^3) of UFP exposure

Associations of UFP and mortality



Per IQR increment (2723 particles/cm^3) of UFP exposure

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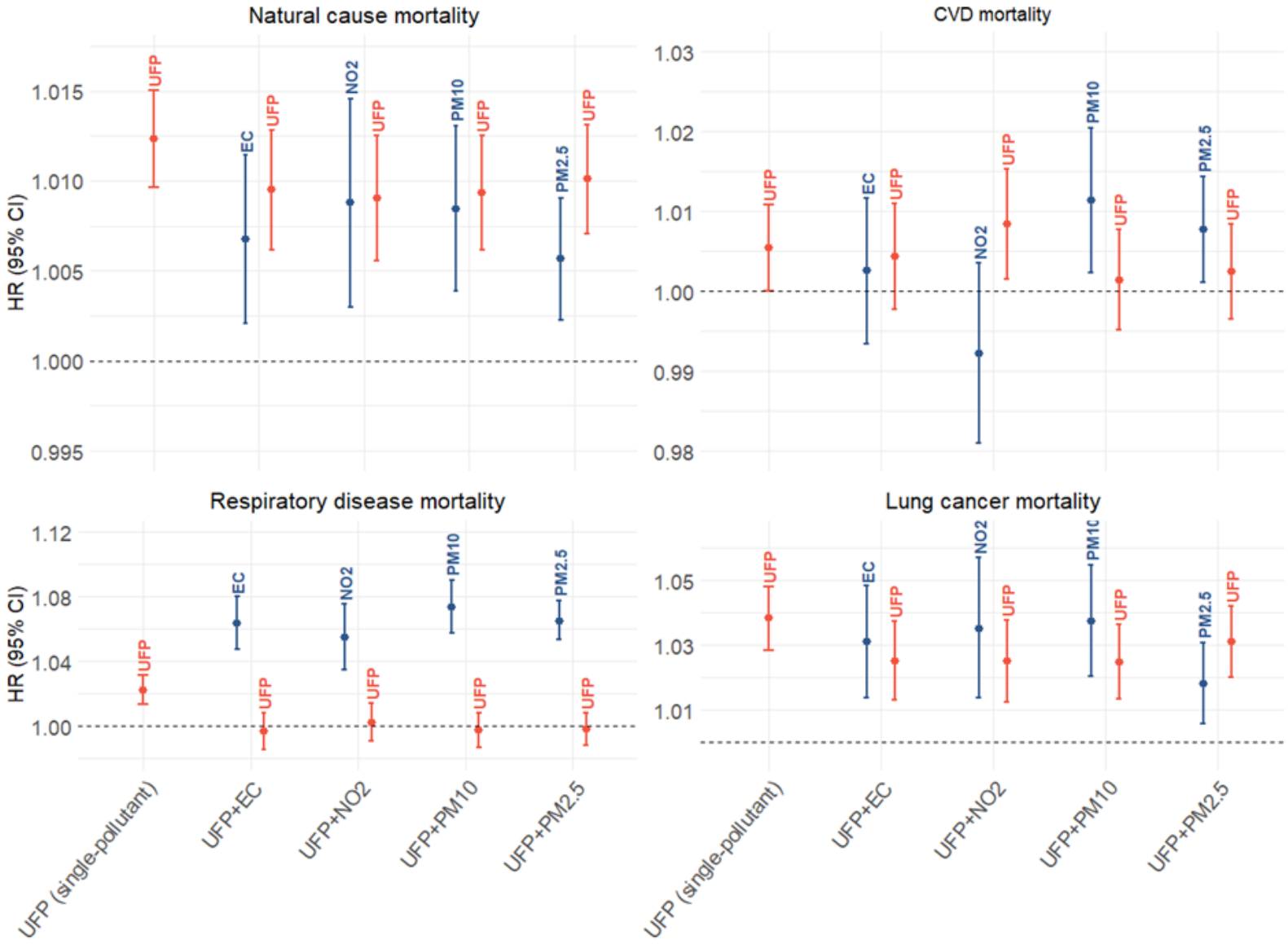
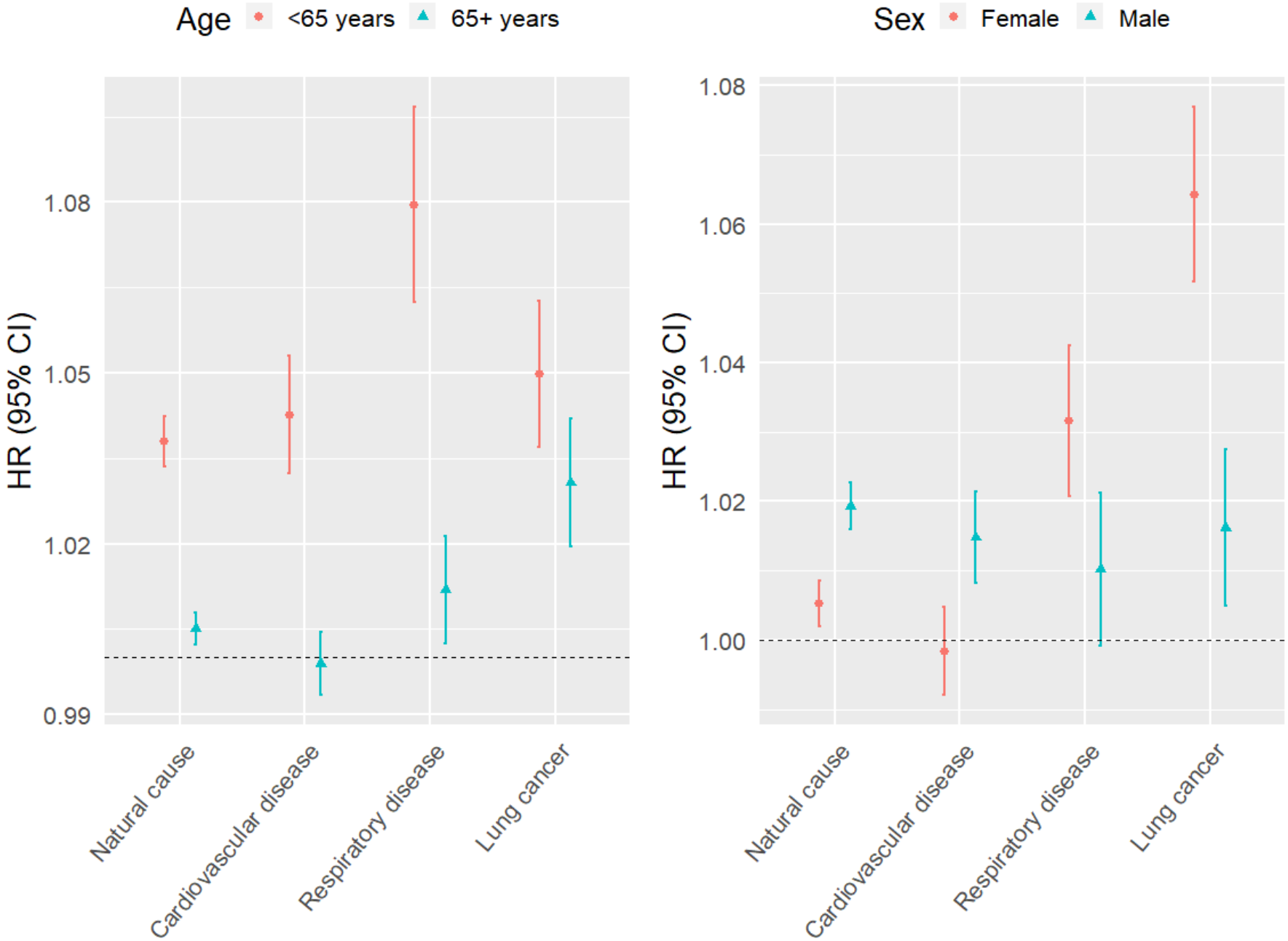
Two-pollutant associations




Age
<65 years
65+ years
HR (95% CI)
1.08
1.05
1.02
0.99
Natural cause
Cardiovascular disease
Respiratory disease
Lung cancer
Sex
Female
Male
HR (95% CI)
1.08
1.06
1.04
1.02
1.00
Natural cause
Cardiovascular disease
Respiratory disease
Lung cancer

Discussion

- Significant associations of long-term UFP exposure with natural cause and lung cancer mortality, independent from co-pollutants
  - Little collinearity in two-pollutant models
  - ➢ Mortality (partly) driven by UFP

Strengths & limitations

- Strengths
  - Exposure assessment in middle of follow-up period
  - Exposure assessment at each residential address separately
  - Large cohort including all adult Dutch citizens
- Limitations
  - Lack of information on individual lifestyle factors, partially accounted for with indirect adjustment for smoking and BMI

Conclusion

- Long-term UFP exposure independently associated with natural and lung cancer mortality in adults
- Air pollution policies might be supplemented with routine measurements and regulations of UFP

Comparison of different exposure models

Exposure assessment method	Monitoring	Domain	Time period
Google Airview	Mobile	Amsterdam	2019-2020
MUSIC	Mobile & short-term	Major cities	2013
Exposomics	Mobile & short-term	Major cities	2014-2015
RUN	Mobile & short-term	Netherlands	2016-2017

UFP model	Lung cancer mortality HR (95% CI)
Google_SLR	1.041 (1.028; 1.054)
Google_RF	1.016 (1.009; 1.024)
Google_LASSO	1.024 (1.014; 1.035)
Exposomics_m_SLR	1.020 (1.011; 1.029)
Exposomics_m_RF	1.026 (1.014; 1.038)
Exposomics_m_LASSO	1.037 (1.024; 1.050)
Exposomics_st_SLR	1.028 (1.019; 1.036)
Exposomics_st_RF	1.041 (1.028; 1.054)
Exposomics_st_LASSO	1.017 (1.011; 1.024)
MUSIC_m_SLR	1.017 (1.008; 1.026)
MUSIC_m_RF	1.018 (1.010; 1.026)
MUSIC_m_LASSO	1.041 (1.028; 1.053)
MUSIC_st_SLR	1.004 (1.002; 1.005)
MUSIC_st_RF	1.028 (1.019; 1.037)
RUN_m_SLR	1.016 (1.010; 1.023)
RUN_m_RF	1.003 (1.000; 1.006)
RUN_m_LASSO	1.017 (1.011; 1.024)
RUN_st_SLR	1.035 (1.024; 1.046)
RUN_st_RF	1.020 (1.013; 1.028)
RUN_st_LASSO	1.038 (1.025; 1.051)

Lung cancer incidence – previous research

- Toronto (Weichental, 2017) -> no association
- Southern California (Jones, 2024) -> modest association with overall lung cancer incidence, stronger association with adenocarcinoma
- Los Angeles county (Bookstein, 2024) -> no association, suggestive for squamous cell carcinoma

Lung cancer incidence – analysis plan

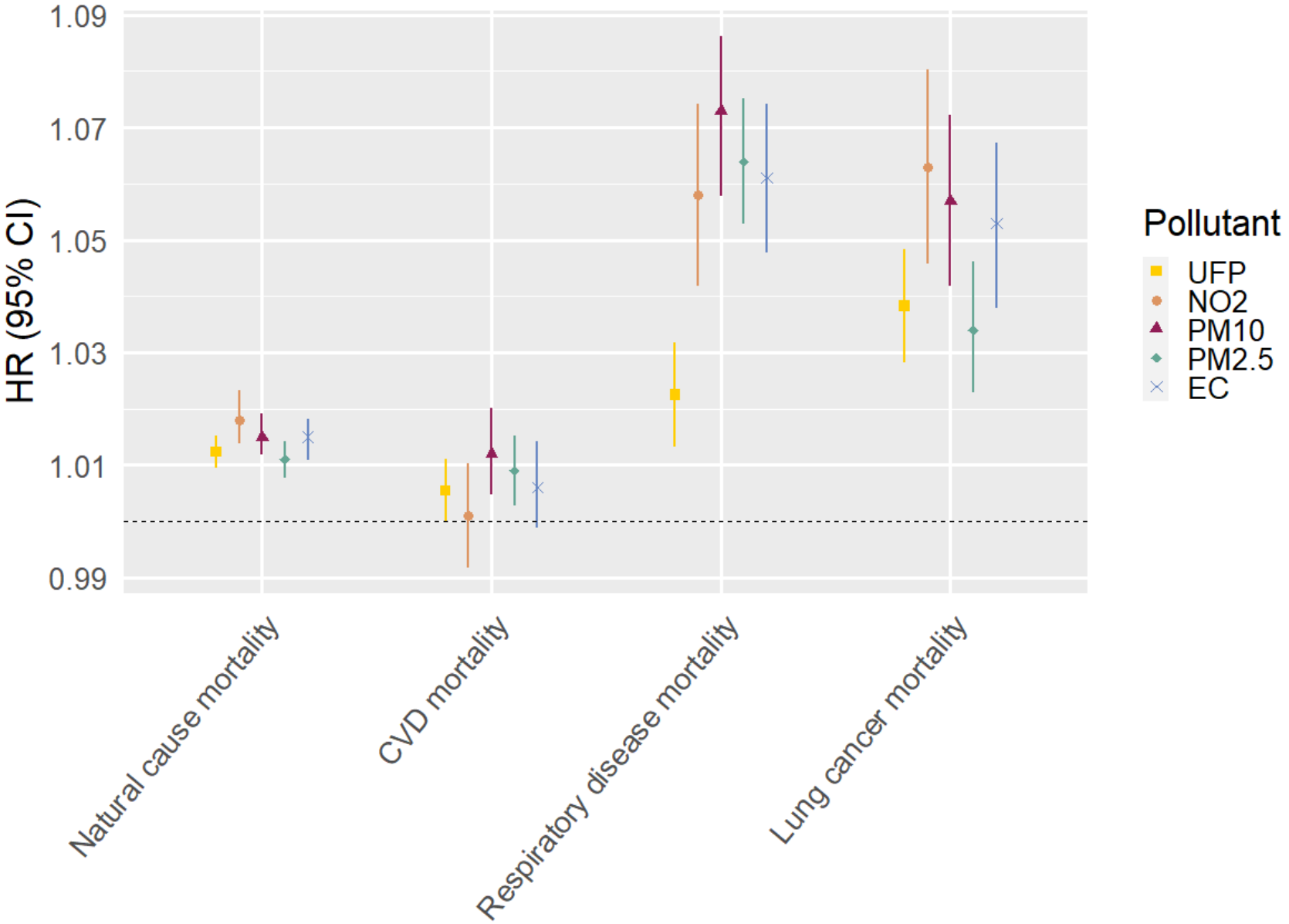
- Administrative cohort, follow-up 2010-2021
- Same UFP exposure
- Lung cancer incidence data from IKNL
- Histological subtypes:
    - Small cell, non-small cell
    - Adenocarcinoma
    - Squamous cell carcinoma

Sharing science,
shaping tomorrow

Nicole Janssen, Joost Wesseling, Sjoerd van Ratingen, Maciek Strak, Jules Kerckhoffs, Ulrike Gehring, Wouter Hendricx, Kees de Hoogh, Roel Vermeulen, Gerard Hoek

Adjusted associations of UFP and co-pollutants with mortality

Per IQR increments of air pollutant exposure



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