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Supplementary appendix

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Supplement to: Wolf K, Hoffmann B, Andersen ZJ, et al. Long-term exposure to low-level ambient air pollution and incidence of stroke and coronary heart disease: a pooled analysis of six European cohorts within the ELAPSE project. *Lancet Planet Health* 2021; **5:** e620–32.

APPENDIX

Long-term exposure to low-level ambient air pollution and incidence of stroke and coronary heart disease – Results from six European cohorts within the ELAPSE Project

Wolf et al. *on behalf of the ELAPSE Project Team*

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Appendix A: Supplementary Methods

Supplementary Methods M1. Cohorts Details

We pooled individual data from six existing population-based cohort studies from four northern European countries:

- Sweden provided data from the Cardiovascular Effects of Air Pollution and Noise in Stockholm (CEANS) study combining four sub-cohorts.
- Denmark contributed with two cohorts: the Diet, Cancer and Health cohort (DCH) and the Danish Nurse Cohort (DNC) including two sub-cohorts.
- The Netherlands provided data from the Dutch European Investigation into Cancer and Nutrition (EPIC-NL) consisting of two sub-cohorts.
- Germany contributed with two cohorts: the Heinz Nixdorf Recall study (HNR) and the Cooperative Health Research in the Region of Augsburg (KORA) study including two sub-cohorts.

Most study areas included larger cities with small surrounding rural communities (CEANS, DCH, HNR, KORA) but some also covered the whole country (DNC, EPIC-MORGEN). Detailed cohort characteristics can be found in Table 1 and Supplementary Table 1.

CEANS (Cardiovascular Effects of Air Pollution and Noise in Stockholm)

The cohort is comprised of four subcohorts: The Stockholm Diabetes Preventive Program (SDPP) is a population-based prospective study of 7,949 subjects aged 35–54 years.[1] The SIXTY subcohort consists of a random population sample of one-third of all men and women living in Stockholm County turning 60 years between August 1997 and March 1999.[2] The Screening Across the Lifespan Twin Study (SALT) sampled 7,043 individuals from the Swedish Twin Register born 1958 and earlier, who lived in Stockholm County.[3] Lastly, The Swedish National Study of Aging and Care in Kungsholmen (SNAC-K) randomly sampled individuals 60+ years of age from a central area in Stockholm.[4]

All participants resided in Stockholm County, Sweden.

Main references:

1. Eriksson AK, Ekbom A, Granath F, et al. Psychological distress and risk of pre-diabetes and Type 2 diabetes in a prospective study of Swedish middle-aged men and women. Diabet Med 2008;25:834–42.

2. Wändell PE, Wajngot A, de Faire U, et al. Increased prevalence of diabetes among immigrants from non-European countries in 60-year-old men and women in Sweden. Diabetes Metab 2007;33:30–6.

3. Lichtenstein P, Sullivan PF, Cnattingius S, et al. The Swedish Twin Registry in the third millennium: an update. Twin Res Hum Genet 2006;9:875–82.

4. Lagergren M, Fratiglioni L, Hallberg IR, et al. A longitudinal study integrating population, care and social services data. The Swedish National study on Aging and Care (SNAC). Aging Clin Exp Res 2004;16:158–68.

Table M1. Characteristics of the Cardiovascular Effects of Air Pollution and Noise in Stockholm (CEANS) cohort

	CEANS, sub-cohorts			
Variable	SDPP	SIXTY	SALT	SNAC-K
Baseline year, range	1992–1998	1997–1999	1998–2002	2001–2004
Enrolled, N[a]	7,835	4,180	6,724	3,248
Exclusions, N[b]	33	135	283	340
Missing on covariates, N[c]	314	231	512	361
Included in CVD incidence analyses, N	7,488	3,814	5,929	2,547
Stroke, N (%)	132 (1·8)	199 (5·2)	241 (4·1)	203 (8·0)
Coronary heart disease, N (%)	238 (3·2)	298 (7·8)	303 (5·1)	210 (8·2)
Age at baseline, yrs (mean ± SD)	47 ± 4·9	60 ± 0	57·4 ± 10·4	72·4 ± 10·3
Women, N (%)	4,582 (61·2)	2,023 (53·0)	3,326 (56·1)	1,580 (62·0)
Employed, N (%)	6,794 (90·7)	2,622 (68·7)	3,902 (65·8)	617 (24·2)
Marital status, N (%)				
Single	1,229 (16·4)	176 (4·6)	827 (13·9)	424 (16·6)
Married	6,259 (83·6)	2,820 (73·9)	4,026 (67·9)	1,194 (46·9)
Divorced	-	620 (16·3)	671 (11·3)	354 (13·9)
Widowed	-	198 (5·2)	405 (6·8)	575 (22·6)
BMI, kg/m^2, N (%)				
< 18·5	51 (0·7)	26 (0·7)	92 (1·6)	68 (2·7)
18·5–24·9	3,588 (47·9)	1,371 (35·9)	3,494 (58·9)	1,112 (43·7)
25·0–29·9	2,913 (38·9)	1,696 (44·5)	1,964 (33·1)	1,041 (40·9)
30·0+	936 (12·5)	721 (18·9)	379 (6·4)	326 (12·8)
Smoking status, N (%)				
Current	1,973 (26·3)	804 (21·1)	1,260 (21·3)	374 (14·7)
Previous	2,720 (36·3)	1,457 (38·2)	1,965 (33·1)	981 (38·5)
Never	2,795 (37·3)	1,553 (40·7)	2,704 (45·6)	1,192 (46·8)
Smoking duration[d], yrs (mean ± SD)	12·6 ± 13	15·2 ± 16·2	14·5 ± 16·8	15·8 ± 19·2
Smoking intensity[d], g/d (mean ± SD)	8·5 ± 8·8	7·9 ± 9·2	7·5 ± 9·7	4·1 ± 6·2
Education, N (%)				
Primary school or less	2,354 (31·4)	1,510 (39·6)	1,556 (26·2)	629 (24·7)
Secondary school	2,879 (38·4)	1,236 (32·4)	2,161 (36·4)	1,019 (40·0)
University degree and more	2,255 (30·1)	1,068 (28)	2,212 (37·3)	899 (35·3)
Neighborhood income[e] (mean ± SD)	24·3 ± 4·2	24·8 ± 6·9	25·3 ± 6·7	28·7 ± 2·2
Noise (Lden, dB; lower cut-off value 45dB), mean ± SD	46·5 ± 3·2	49·6 ± 6·2	50 ± 6·4	58·6 ± 6·7
Missing, N (%)	0	0	0	0

[a]Number of participants for which information was transferred to Utrecht University for pooling.
[b]Due to failed exposure assignment or a history of either stroke or CHD at least three years before baseline.
[c]Main model 3: age, sex, year of baseline visit, smoking status, duration, intensity, $intensity^2$, BMI, marital status, employment status, education and 2001 mean income at the neighborhood level.
[d]Among current and former smokers.
[e]EUR per 1,000, year 2001.

DCH (Diet, Cancer and Health)

Participants were recruited among persons aged 50-64 years from the areas of greater Copenhagen and Aarhus, Denmark, who were born in Denmark and free of cancer at baseline.

Main reference:

Tjonneland A, Olsen A, Boll K et al. Study design, exposure variables, and socioeconomic determinants of participation in Diet, Cancer and Health: a population-based prospective cohort study of 57,053 men and women in Denmark. Scand J Public Health 2007; 35: 432–41

Table M2. Characteristics of the Diet, Cancer and Health (DCH) cohort

Variable	**DCH**
Baseline year, range	1993-1997
Enrolled, N[a]	56,308
Exclusions[b]	1,500
Missing on covariates[c]	2,720
Included in CVD incidence analyses	52,088
Stroke, N (%)	4,116 (7·9)
Coronary heart disease, N (%)	4,374 (8·4)
Age at baseline, yrs (mean ± SD)	56·6 ± 4·3
Women, N (%)	27,657 (53·1)
Employed, N (%)	41,063 (78·8)
Marital status, N (%)	
Single	3,177 (6·1)
Married	37,288 (71·6)
Divorced	8,765 (16·8)
Widowed	2,858 (5·5)
BMI, kg/m^2, N (%)	
< 18·5	408 (0·8)
18·5–24·9	22,656 (43·5)
25·0–29·9	21,582 (41·4)
30·0+	7,442 (14·3)
Smoking status, N (%)	
Current	18,785 (36·1)
Previous	14,353 (27·6)
Never	18,950 (36·4)
Smoking duration[d], yrs (mean ± SD)	18·8 ± 17·1
Smoking intensity[d], g/d (mean ± SD)	10·3 ± 11·2
Education, N (%)	
Primary school or less	7,664 (14·7)
Secondary school	32,887 (63·1)
University degree and more	11,537 (22·1)
Neighborhood income[e] (mean ± SD)	20·2 ± 3·4
Noise (Lden, dB; lower cut-off value 45dB), mean ± SD	57·8 ± 6·8
Missing, N (%)	39 (0·1)

[a]Number of participants for which information was transferred to Utrecht University for pooling.
[b]Due to failed exposure assignment or a history of either stroke or CHD at least three years before baseline.
[c]Main model 3: age, sex, year of baseline visit, smoking status, duration, intensity, intensity^2, BMI, marital status, employment status, education and 2001 mean income at the neighborhood level.
[d]Among current and former smokers.
[e]EUR per 1,000, year 2001.

DNC (Danish Nurse Cohort)

The cohort was sampled among members of The Danish Nurse Organization (DNO) including both working and retired nurses. Questionnaires were mailed in 1993 to members aged 45+ years and again in 1999 with the inclusion of new members (45+ years).

Main reference:

Hundrup YA, Simonsen M, Jørgensen T, Obel EB. Cohort profile: The Danish Nurse Cohort. International Journal of Epidemiology, 2012;41:1241–47.

Table M3. Characteristics of the Danish Nurse Cohort (DNC)

	DNC, sub-cohorts	
Variable	DNC-1993	DNC-1999
Baseline year, range	1993	1999
Enrolled, N[a]	19,664	8,769
Exclusions[b]	287	81
Missing on covariates[c]	2,567	633
Included in CVD incidence analyses	16,810	8,055
Stroke, N (%)	1,009 (6·0)	101 (1·3)
Coronary heart disease, N (%)	1,802 (10·7)	335 (4·2)
Age at baseline, yrs (mean ± SD)	56·1 ± 8·4	47·9 ± 4·0
Women, N (%)	16,810 (100)	8,055 (100)
Employed, N (%)	11,856 (70·5)	7,655 (95·0)
Marital status, N (%)		
Single	1,765 (10·5)	750 (9·3)
Married	11,406 (67·9)	6,114 (75·9)
Divorced	2,087 (12·4)	1,032 (12·8)
Widowed	1,552 (9·2)	159 (2·0)
BMI, kg/m^2, N (%)		
< 18·5	492 (2·9)	137 (1·7)
18·5–24·9	11,613 (69·1)	5,514 (68·5)
25·0–29·9	3,841 (22·8)	1,871 (23·2)
30·0+	864 (5·1)	533 (6·6)
Smoking status, N (%)		
Current	6,304 (37·5)	2,309 (28·7)
Previous	4,768 (28·4)	2,618 (32·5)
Never	5,738 (34·1)	3,128 (38·8)
Smoking duration[d], yrs (mean ± SD)	16·4 ± 15·8	12·5 ± 12·7
Smoking intensity[d], g/d (mean ± SD)	8·3 ± 9·3	7·5 ± 8·4
Education, N (%)		
Primary school or less	0 (0)	0 (0)
Secondary school	0 (0)	0 (0)
University degree and more	16,810 (100)	8,055 (100)
Neighborhood income[e] (mean ± SD)	19·2 ± 2·6	19·0 ± 2·3
Noise (Lden, dB; lower cut-off value 45dB), mean ± SD	52·8 ± 6·5	52·6 ± 6·5
Missing, N (%)	0	0

[a]Number of participants for which information was transferred to Utrecht University for pooling.
[b]Due to failed exposure assignment or a history of either stroke or CHD at least three years before baseline.
[c]Main model 3: age, sex, year of baseline visit, smoking status, duration, intensity, intensity^2, BMI, marital status, employment status, education and 2001 mean income at the neighborhood level.
[d]Among current and former smokers.
[e]EUR per 1,000, year 2001.

EPIC-NL (European Prospective Investigation into Cancer and Nutrition, the Netherlands)

The EPIC-NL combines two Dutch EPIC-cohorts: The Monitoring Project on Risk Factors and chronic diseases in the Netherlands (MORGEN) cohort which consists of a general population sample aged 20–59 years from three Dutch towns (Amsterdam, Doetinchem and Maastricht). Prospect is a prospective cohort study among women aged 49–70, residing in the city of Utrecht or its vicinity, who participated in the nation wide Dutch breast cancer screening programme between 1993 and 1997.

Main reference:

Beulens JWJ, Monninkhof EM, Verschuren WMM et al. Cohort Profile: The EPIC-NL study. International Journal of Epidemiology 2010; 39: 1170–78.

Table M4. Characteristics of the European Prospective Investigation into Cancer and Nutrition, the Netherlands (EPIC-NL)

	EPIC-NL, sub-cohorts	
Variable	MORGEN	PROSPECT
Baseline year, range	1993-97	1993-97
Enrolled, N[a]	20,711	16,194
Exclusions[b]	696	400
Missing on covariates[c]	2,372	1,590
Included in CVD incidence analyses	17,643	14,204
Stroke, N (%)	280 (1·6)	444 (3·1)
Coronary heart disease, N (%)	1,127 (6·4)	1,055 (7·4)
Age at baseline, yrs (mean ± SD)	42·9 ± 11·2	57·6 ± 6
Women, N (%)	9,718 (55·1)	14,204 (100)
Employed, N (%)	12,179 (69)	7,264 (51·1)
Marital status, N (%)		
Single	4,414 (25)	815 (5·7)
Married	11,552 (65·5)	10,908 (76·8)
Divorced	1,324 (7·5)	1,139 (8·0)
Widowed	353 (2)	1,342 (9·4)
BMI, kg/m^2, N (%)		
< 18·5	181 (1)	84 (0·6)
18·5–24·9	8,794 (49·8)	6,351 (44·7)
25·0–29·9	6,648 (37·7)	5,650 (39·8)
30·0+	2,020 (11·4)	2,119 (14·9)
Smoking status, N (%)		
Current	6,121 (34·7)	3273 (23·0)
Previous	4,973 (28·2)	4,662 (32·8)
Never	6,549 (37·1)	6,269 (44·1)
Smoking duration[d], yrs (mean ± SD)	13·4 ± 13·4	15·5 ± 16·6
Smoking intensity[d], g/d (mean ± SD)	10·1 ± 11·1	6·3 ± 8·3
Education, N (%)		
Primary school or less	1,985 (11·3)	3,146 (22·1)
Secondary school	14,286 (81·0)	10,549 (74·3)
University degree and more	1372 (7·8)	509 (3·6)
Neighborhood income[e] (mean ± SD)	12·1 ± 1·6	13·1 ± 1·4
Noise (Lden, dB; lower cut-off value 45dB), mean ± SD	-	-
Missing, N (%)	-	-

[a]Number of participants for which information was transferred to Utrecht University for pooling.
[b]Due to failed exposure assignment or a history of either stroke or CHD at least three years before baseline.
[c]Main model 3: age, sex, year of baseline visit, smoking status, duration, intensity, intensity^2, BMI, marital status, employment status, education and 2001 mean income at the neighborhood level.
[d]Among current and former smokers.
[e]EUR per 1,000, year 2001.

HNR (Heinz Nixdorf Recall study)

The cohort consists of randomly sampled persons aged 45 to 75 years from the Ruhr area, Germany primarily in the three adjacent large cities Bochum, Essen, and Mülheim.

Main references:

Schmermund A, Möhlenkamp S, Stang A et al. Assessment of clinically silent atherosclerotic disease and established and novel risk factors for predicting myocardial infarction and cardiac death in healthy middle-aged subjects: Rationale and design of the Heinz Nixdorf RECALL Study. American Heart Journal, 2002; 144: 212–2018.

Erbel R, Mohlenkamp S, Moebus S, et al. Coronary risk stratification, discrimination, and reclassification improvement based on quantification of subclinical coronary atherosclerosis: the Heinz Nixdorf Recall study. Journal of the American College of Cardiology 2010; 56(17): 1397-406.

Table M5. Characteristics of the Heinz Nixdorf Recall study (HNR)

Variable	**HNR**
Baseline year, range	2000-2003
Enrolled, N[a]	4,809
Exclusions[b]	363
Missing on covariates[c]	71
Included in CVD incidence analyses	4,375
Stroke, N (%)	129 (2·9)
Coronary heart disease, N (%)	193 (4·4)
Age at baseline, yrs (mean ± SD)	59·3 ± 7·7
Women, N (%)	2,280 (52·1)
Employed, N (%)	1,830 (41·8)
Marital status, N (%)	
Single	251 (5·7)
Married	3,277 (74·9)
Divorced	440 (10·1)
Widowed	407 (9·3)
BMI, kg/m^2, N (%)	
< 18·5	14 (0·3)
18·5–24·9	1,173 (26·8)
25·0–29·9	2,011 (46·0)
30·0+	1,177 (26·9)
Smoking status, N (%)	
Current	1,037 (23·7)
Previous	1,442 (33·0)
Never	1,896 (43·3)
Smoking duration[d], yrs (mean ± SD)	14·6 ± 15·9
Smoking intensity[d], g/d (mean ± SD)	11·9 ± 16·4
Education, N (%)	
Primary school or less	494 (11·3)
Secondary school	2,432 (55·6)
University degree and more	1,449 (33·1)
Neighborhood income[e] (mean ± SD)	25·3 ± 8·2
Noise (Lden, dB; lower cut-off value 45dB), mean ± SD	54·6 ± 8·6
Missing, N (%)	30 (0·7)

[a]Number of participants for which information was transferred to Utrecht University for pooling.
[b]Due to failed exposure assignment or a history of either stroke or CHD at least three years before baseline.
[c]Main model 3: age, sex, year of baseline visit, smoking status, duration, intensity, intensity^2, BMI, marital status, employment status, education and 2001 mean income at the neighborhood level.
[d]Among current and former smokers.
[e]EUR per 1,000, year 2001.

KORA (Cooperative Health Research in the Region of Augsburg)

Two cross-sectional population-representative surveys were conducted in 1994-1995 (S3 survey) and 1999-2001 (survey S4) in the city of Augsburg and two adjacent rural counties including inhabitants of German nationality aged 25 to 74.

Main reference:

Holle R, Happich M, Lowel H, Wichmann HE. KORA--a research platform for population based health research. Gesundheitswesen 2005; 67 Suppl 1: S19-S25.

Table M6. Characteristics of the Cooperative Health Research in the Region of Augsburg (KORA) cohort

	KORA, sub-cohorts	
Variable	KORA-S3	KORA-S4
Baseline year, range	1994-1995	1999-2001
Enrolled, N[a]	4,566	4,257
Exclusions[b]	656	510
Missing on covariates[c]	1,728	1,734
Included in CVD incidence analyses	2,182	2,013
Stroke, N (%)	53 (2·4)	43 (2·1)
Coronary heart disease, N (%)	66 (3·0)	70 (3·5)
Age at baseline, yrs (mean ± SD)	48·7 ± 13·1	48·8 ± 13·4
Women, N (%)	1,124 (51·5)	1,068 (53·1)
Employed, N (%)	1,286 (58·9)	1,241 (61·6)
Marital status, N (%)		
Single	193 (8·8)	155 (7·7)
Married	1,784 (81·8)	1,608 (79·9)
Divorced	88 (4·0)	132 (6·6)
Widowed	117 (5·4)	118 (5·9)
BMI, kg/m^2, N (%)		
< 18·5	12 (0·5)	7 (0·3)
18·5–24·9	746 (34·2)	650 (32·3)
25·0–29·9	949 (43·5)	878 (43·6)
30·0+	475 (21·8)	478 (23·7)
Smoking status, N (%)		
Current	438 (20·1)	459 (22·8)
Previous	620 (28·4)	626 (31·1)
Never	1,124 (51·5)	928 (46·1)
Smoking duration[d], yrs (mean ± SD)	9·5 ± 12·7	10·6 ± 13·1
Smoking intensity[d], g/d (mean ± SD)	7·7 ± 12·6	9·3 ± 13·5
Education, N (%)		
Primary school or less	307 (14·1)	209 (10·4)
Secondary school	1,564 (71·7)	1,407 (69·9)
University degree and more	311 (14·3)	397 (19·7)
Neighborhood income[e] (mean ± SD)	36·8 ± 4·4	38·1 ± 7·4
Noise (Lden, dB; lower cut-off value 45dB), mean ± SD	54 ± 5·9	53·9 ± 5·8
Missing, N (%)	1 (0·0)	6 (0·3)

[a]Number of participants for which information was transferred to Utrecht University for pooling.
[b]Due to failed exposure assignment or a history of either stroke or CHD at least three years before baseline.
[c]Main model 3: age, sex, year of baseline visit, smoking status, duration, intensity, intensity^2, BMI, marital status, employment status, education and 2001 mean income at the neighborhood level.
[d]Among current and former smokers.
[e]EUR per 1,000, year 2001.

Supplementary Methods M2. Outcome definition

Stroke was defined following criteria based on the International Classification of Diseases (ICD), 8^{th}, 9^{th} and 10^{th} revisions codes including hospitalization with principal diagnosis of ischemic, haemorrhagic or unspecified stroke (ICD8: 431-434, 436; ICD9: 431, 433.x1, 434, 436; ICD10: I61, I63, I64) and out-of-hospital deaths from cerebrovascular diseases (ICD9: 431-436; ICD10: I61-I64). Acute coronary heart disease was defined as hospitalizations with principal diagnosis of acute myocardial infarction or other acute and sub-acute forms of ischemic heart disease (ICD-8: 410, 411, 4272; ICD-9: 410, 411, 427.5; ICD-10: I20.0, I21, I22, I23, I46) and out-of-hospital deaths from ischemic heart diseases (ICD-9: 410-414, 427.5; ICD-10: I20-I25, I46). The ICD8 coding was only used by the Danish cohorts until 1993 and is therefore specified for hospitalizations only since most deaths in the DNC and all deaths in the DCH cohorts occurred after 1993. The few fatal events in DNC before 1994 were translated manually from ICD-8 into ICD-10. For the German cohorts, outcome identification was accomplished by interview and inspection of medical records and death certificates. For HNR, cardiovascular outcomes were determined by an independent endpoint committee based on self-reports, physician and next-of-kin interviews, and medical records (Schmermund et al. 2002). We defined the following outcomes for the analysis: 1. First occurrence of stroke. 2. First occurrence of a coronary heart disease (CHD) event, defined as a non-fatal myocardial infarction or cardiac death (MI) (Rodins et al. 2020, Schmermund et al. 2002). For KORA, survival was ascertained for S3 participants in 2011 through Population Registry search. Survival of S4 participants was ascertained through a combination of returned questionnaires and subsequent Population Registry search or follow up examinations and is available from recruitment until 2013/2014. Causes of death are recorded for all deaths from the death certificates. Morbidity follow up was tracked via questionnaires sent by mail (2009 for S3 and S4) and questionnaires at follow up examinations (2013/14 for S4). Cases were validated based on hospital records and primary care physician records as well as the MONICA/KORA myocardial infarction registry (Holle et al. 2005, Löwel et al. 2005). We excluded prevalent cases of either stroke or coronary event at least three years before enrolment.

References:

Holle, R., M. Happich, H. Lowel, and H. E. Wichmann. 2005. "KORA--a research platform for population based health research." *Gesundheitswesen* 67 Suppl 1:S19-S25.

Löwel, H., C. Meisinger, M. Heier, and A. Hörmann. 2005. "The population-based acute myocardial infarction (AMI) registry of the MONICA/KORA study region of Augsburg." *Gesundheitswesen* 67 Suppl 1:S31-S37.

Rodins, V., S. Lucht, S. Ohlwein, F. Hennig, V. Soppa, R. Erbel, K. H. Jockel, C. Weimar, D. M. Hermann, S. Schramm, S. Moebus, U. Slomiany, and B. Hoffmann. 2020. "Long-term exposure to ambient source-specific particulate matter and its components and incidence of cardiovascular events - The Heinz Nixdorf Recall study." *Environ Int* 142:105854. doi: 10.1016/j.envint.2020.105854.

Schmermund, A., S. Mohlenkamp, A. Stang, D. Gronemeyer, R. Seibel, H. Hirche, K. Mann, W. Siffert, K. Lauterbach, J. Siegrist, K. H. Jockel, and R. Erbel. 2002. "Assessment of clinically silent atherosclerotic disease and established and novel risk factors for predicting myocardial infarction and cardiac death in healthy middle-aged subjects: rationale and design of the Heinz Nixdorf RECALL Study. Risk Factors, Evaluation of Coronary Calcium and Lifestyle." *American heart journal* 144 (2):212-8.

Supplementary Methods M3. Detailed exposure assessment and procedure for back-extrapolation

We selected 2010 as the primary year of modelling since this was the earliest year of a sufficiently wide coverage of $PM_{2.5}$ monitoring across Europe. For BC, 2009-2010 was the period of ESCAPE monitoring which we used to develop BC models. For reasons of consistency, we used 2010 for NO_2 and O_3 as well for our main models.

As predictor variables, we used road and land use data supplemented with satellite data and dispersion model estimates (de Hoogh et al. 2018):

Satellite derived air pollution data:

- SAT $PM_{2.5}$ estimates at 0.1° x 0.1° (~10 km) and 0.01° x 0.01° (~1 km) resolution derived from global datasets (van Donkelaar et al. 2015) that were constructed based on Aerosol Optical Density (AOD) from multiple satellite products (MISR, MODIS Dark Target, MODIS and SeaWiFS Deep Blue, and MODIS MAIAC) and related to ground-level concentrations using the global GEOS-Chem model.
- SAT NO_2 estimates at 0.1° x 0.1° (~10 km) resolution derived from the tropospheric NO_2 columns measured with the OMI (Ozone Monitoring Instrument) on board the Aura satellite and related to ground-level concentrations using the global GEOS-Chem model.

Chemical transport model (CTM) data:

- Annual $PM_{2.5}$, NO_2 and O_3 estimates derived from the MACC-II ENSEMBLE model at a 0.1º x 0.1º (~10km) resolution
- Annual $PM_{2.5}$, NO_2, BC and O_3 estimates derived from the Danish Eulerian Hemispheric Model (DEHM) at a monthly (temporal) 26 x 26km (spatial) resolution (downscaled from an original 50 x 50km resolution using bi-linear interpolation)

Other predictor variables:

- Road data, classified as 'all' and 'major' roads, extracted from the 1:10,000 EuroStreets digital road network
- Land cover extracted from European Corine Land Cover 2006 data
- Elevation extracted from the SRTM Digital Elevation Database version 4.1 (approximately 90 m resolution).
- Population data (1 km resolution) for 2011 from Eurostat

Land use regression models were developed using the supervised linear regression (SLR) approach used within ESCAPE (Eeftens et al. 2012). Models were validated using five-fold cross-validation and for $PM_{2.5}$ and NO_2 on ESCAPE external data. Five models were developed, each built on 80% of the monitoring sites with the remaining 20% used for validation (sites selected at random, stratified by site type and country). We explored universal kriging or if not feasible X and Y coordinates to further explain spatial variation in the residuals. Kriging significantly improved the $PM_{2.5}$ and O_3 models. Over all our models including kriging explained 66%, 58%, 51% and 60% of the variability in measured concentrations in 5-fold cross-validation for $PM_{2.5}$, NO_2, BC and O_3 respectively. Maps of the pollutant concentrations can be found in Figure M1 below.

We also compared the performance of our SLR approach to 15 algorithms including machine learning methods (random forest, gradient boosting, neural network) and data regularization methods (elastic net, lasso) to develop LUR models for $PM_{2.5}$ and NO_2 (Chen et al. 2019). We observed that the performance of most algorithms was similar, with little indication of better performance of more sophisticated algorithms compared to SLR.

Several studies showed that spatial variation of air pollution concentrations are reasonably stable for up to 10 years (Cesaroni et al. 2012, Eeftens et al. 2011, Gulliver et al. 2013, Wang et al. 2013). To test for spatial stability of our pollution surfaces, we also developed NO_2 and O_3 models for the years 2005 and 2000 and a $PM_{2.5}$ model for the year 2013 (Figure M1; sufficient $PM_{2.5}$ monitoring sites for LUR modelling in Europe are only available from around 2008, with the highest number so far recorded in 2013) (de Hoogh et al. 2018). Agreement in spatial variation was generally high at the overall EU country and combined ELAPSE country level (> 76%) for all comparisons except cold season O3 (Table 4 of (de Hoogh et al. 2018)). Additionally, we compared the measured average concentrations for those stations with measurements going sufficiently back in time between 2010 and 2005 and 2000 (Table 5 of (de Hoogh et al. 2018)). The measured concentrations between the different years yielded high correlations (> 68%). When focusing on ELAPSE participating countries, high correlations were also observed for the majority of the countries and years. We thus assume that the spatial variability of the relevant pollution concentrations remained reasonably stable to the baseline period (year 1992–2004).

We estimated pollutant concentrations for each year from recruitment to end of follow-up for $PM_{2.5}$, NO_2, BC and O_3 via back-extrapolation. For that, we used trends predicted by the Danish Eulerian Hemispheric Model (DEHM; Brandt et al. 2012) providing monthly average concentrations across Europe from 1979 to 2015 at 26 km*26 km spatial resolution (downscaled from an original 50 x 50km resolution using bi-linear interpolation). To allow for varying trends per country and cohort, we calculated population-weighted average concentrations of 26 x 26 km cells in the approximated study area and applied these to the participants' residential concentrations using both the absolute difference and the ratio between annual average concentrations and 2010 exposures from our main model. 2011 European population estimates at the 1x1km level were obtained from GEOSTAT (GEOSTAT-grid-POP-1K-2011-V2-0-1.zip downloaded from http://ec.europa.eu/eurostat/web/gisco/geodata/reference-data/population-distributiondemography/geostat).

The rationale to perform back-extrapolation by modelled concentrations was the consistent availability of estimates across Europe for the full study period for all pollutants. In contrast, routine monitoring was less consistent, not available for BC and only available from about 2008 for $PM_{2.5}$ (Figure M2). We used monitoring data to compare temporal patterns of modelled and measured concentrations for countries with measurements. Although absolute levels varied, time trends generally agreed well between modelled and measured concentrations for NO_2 and O_3: a fairly large downward trend for NO_2 (Figure M3) and a small downward trend for O_3 (Figure M4). For $PM_{2.5}$ (Figure M5), the trends of measured and modelled concentrations agreed well in some countries (the Netherlands, Switzerland) but not in other countries (France, Belgium). The number of sites (2 in France and 1 in Belgium) was too small to draw meaningful conclusions. Given the regional nature of $PM_{2.5}$, very different trends across neighboring countries (e.g. Netherlands and Belgium) are unlikely.

Figure M1. Mapping of Western Europe land use regression models for $PM_{2.5}$, NO_2, BC and warm season O_3 at 100 × 100 m (µg/m^3, BC 10^{-5} m^{-1}). Figure 1E from de Hoogh, K., et al. (2018). "Spatial PM2.5, NO2, O3 and BC models for Western Europe – Evaluation of spatiotemporal stability." Environ Int 120: 81-92.

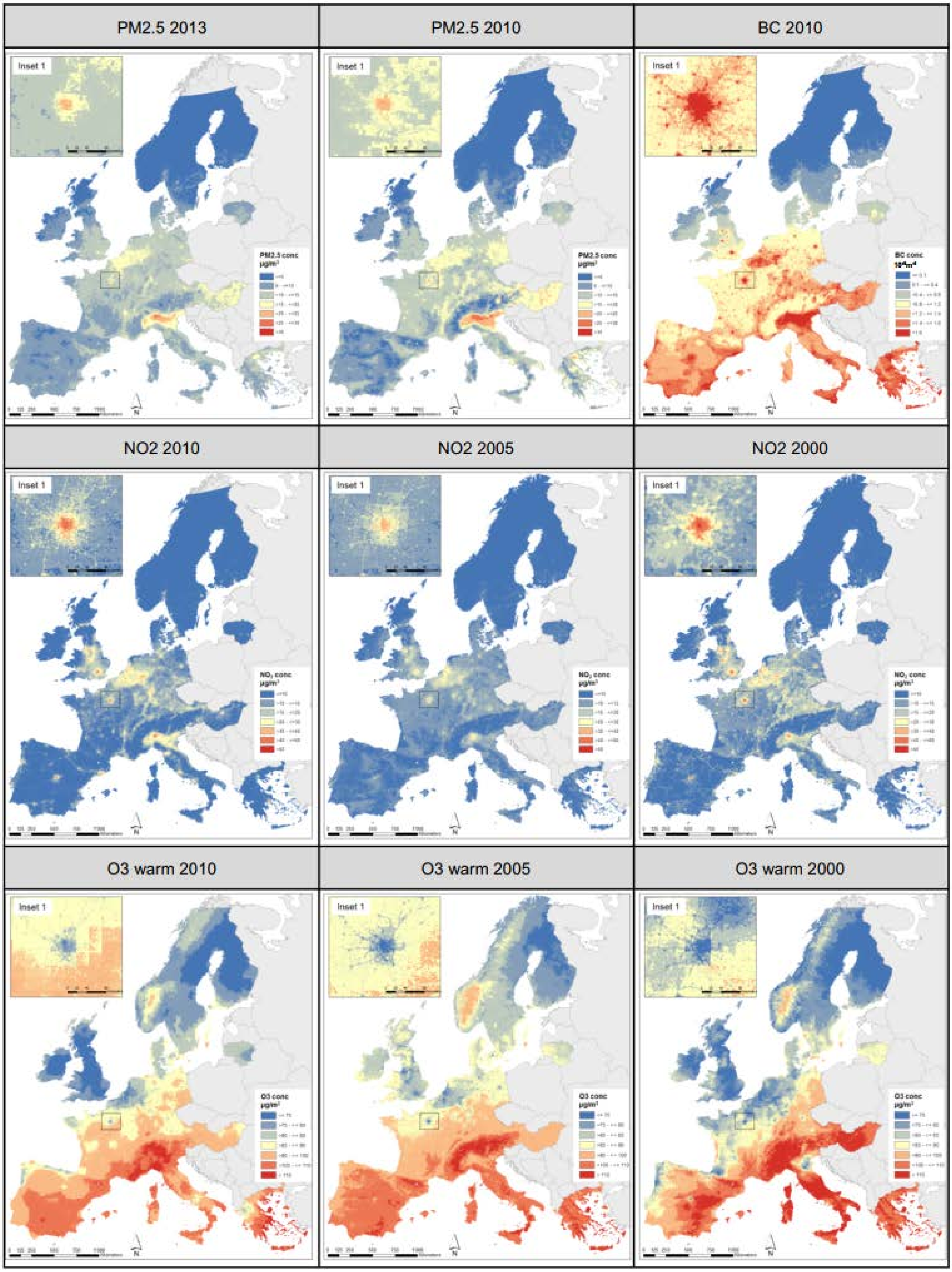


Figure M2: Trends of number of monitoring sites in Europe

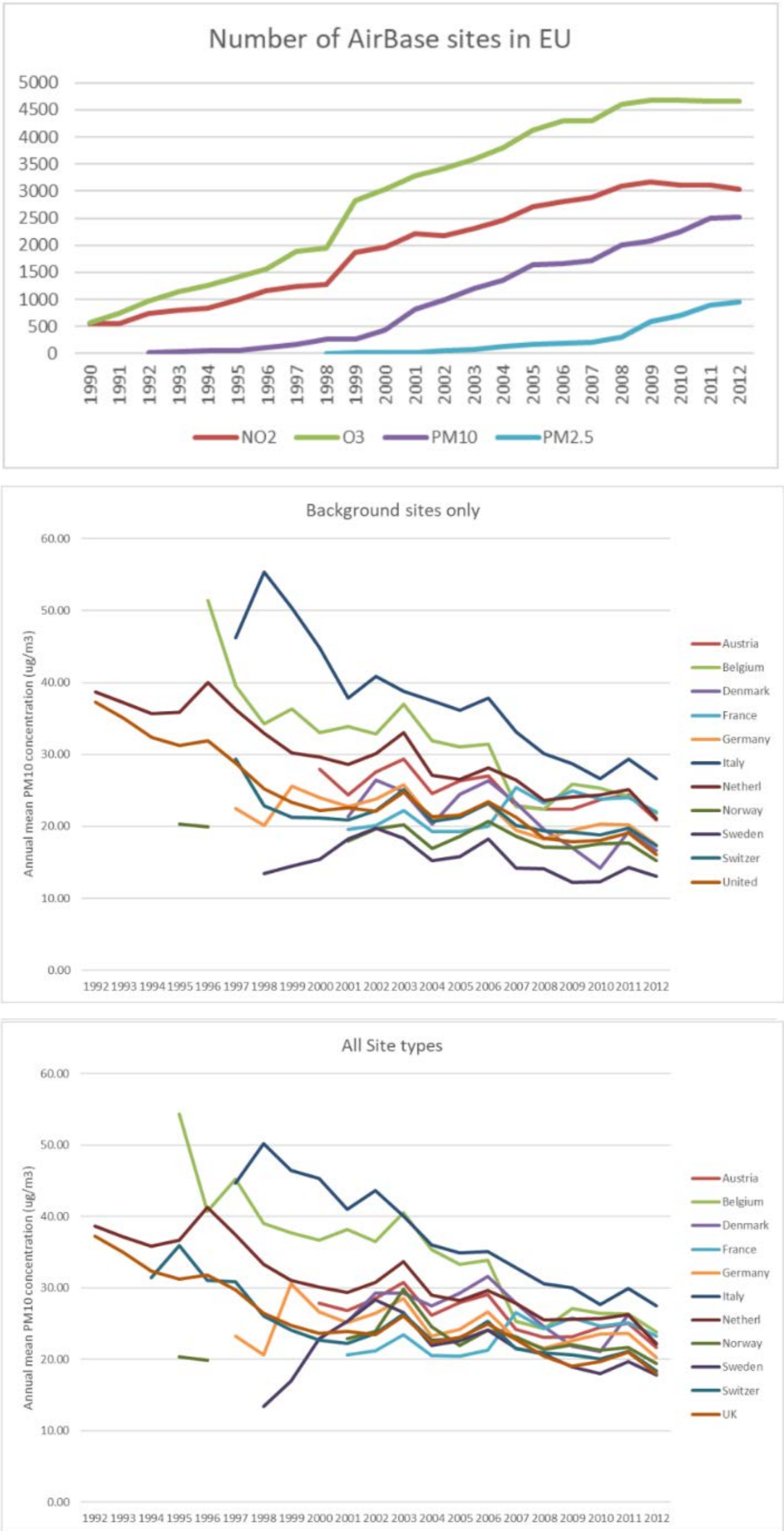


Figure M3: Comparing temporal trends between AIRBASE and DEHM NO_2 for ELAPSE administrative study areas

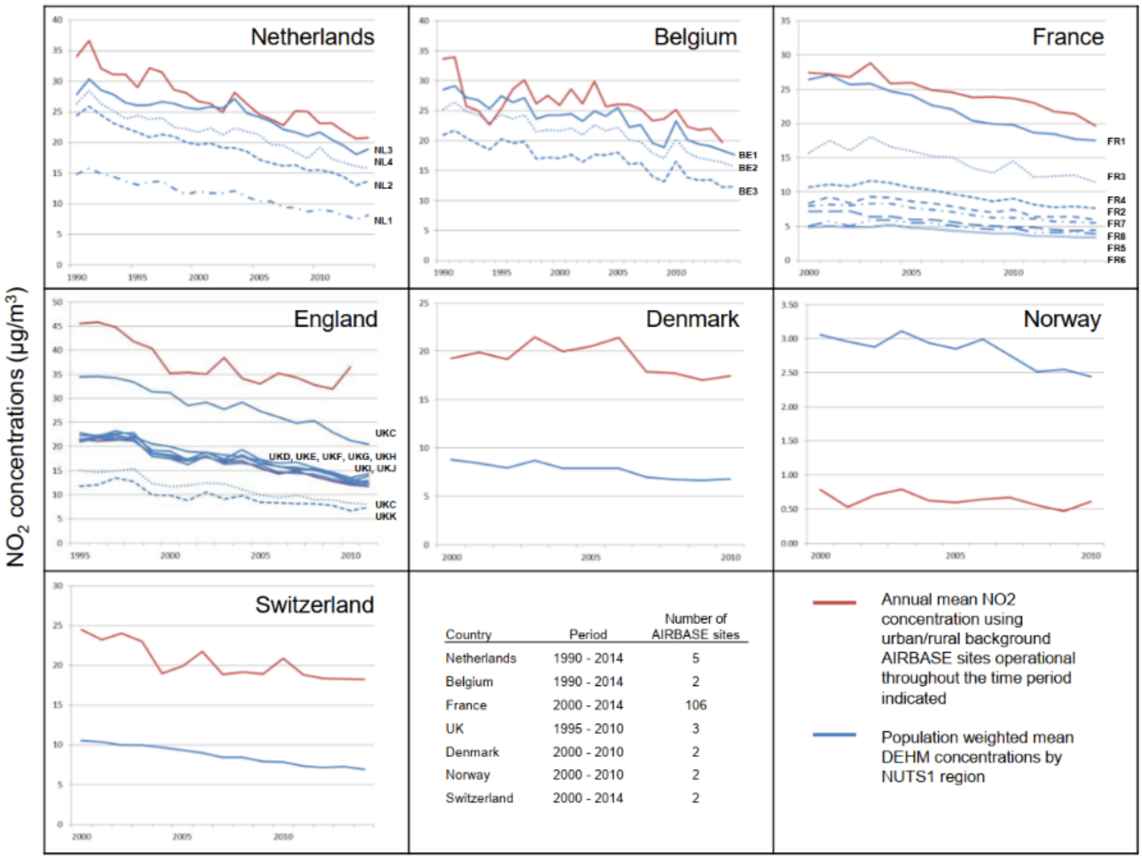


Figure M4: Comparing temporal trends between AIRBASE and DEHM O_3 data for ELAPSE administrative study areas

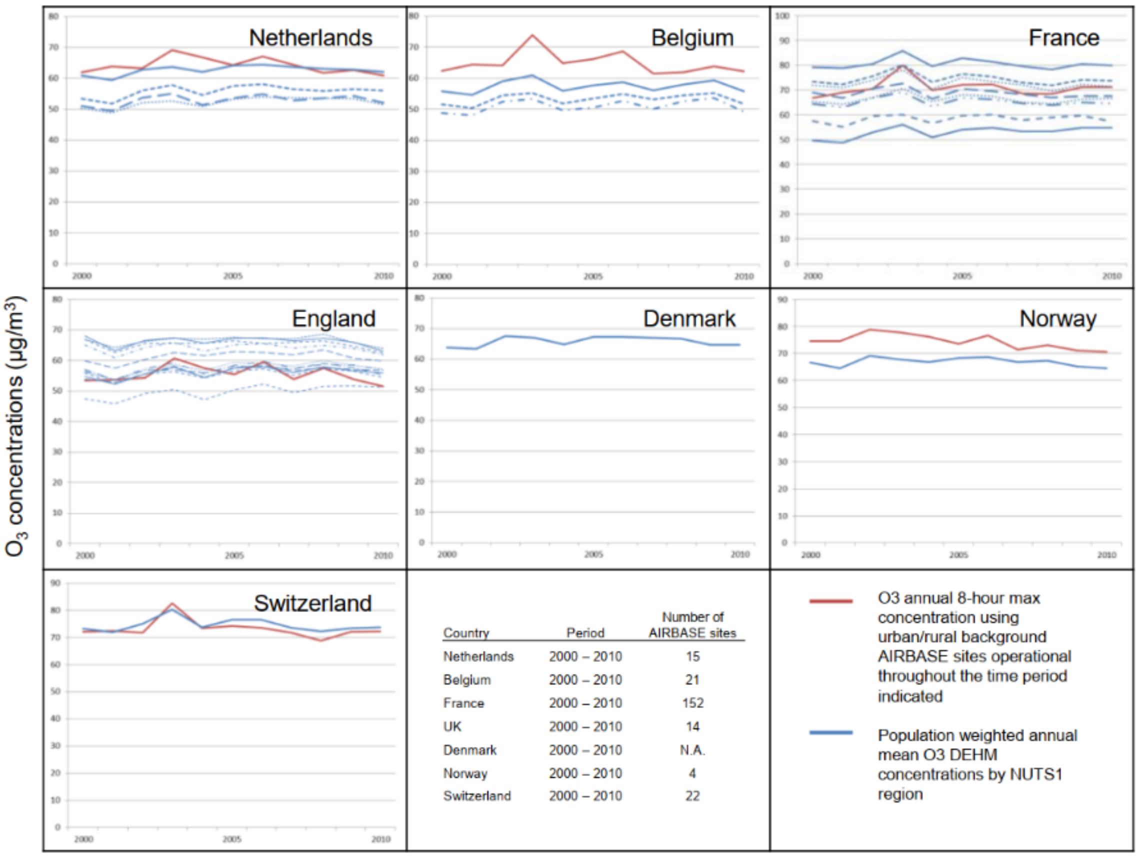
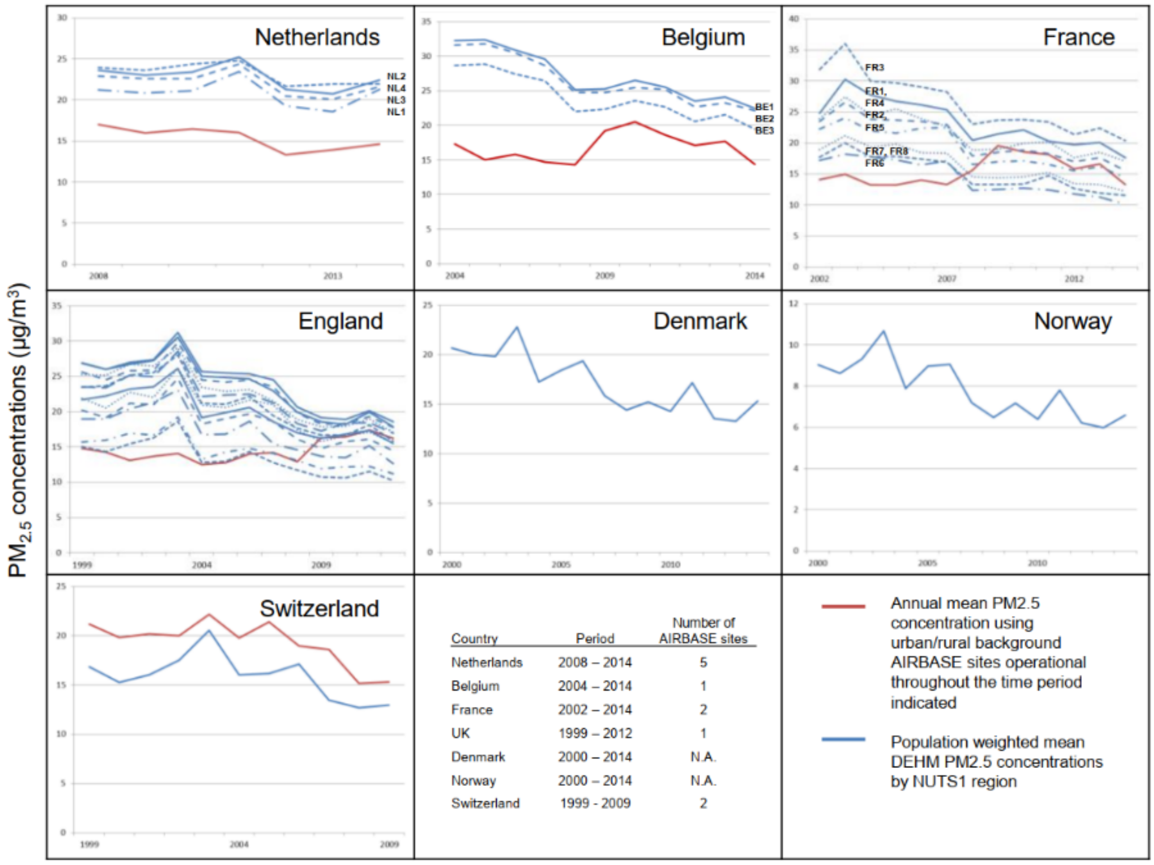


Figure M5: Comparing temporal trends between AIRBASE and DEHM $PM_{2.5}$ for ELAPSE administrative study areas



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Supplementary Methods M4. Shape Constrained Health Impact Function (SCHIF)

The Shape Constrained Health Impact Function (SCHIF) framework was suggested by Nasari and colleagues (Nasari et al. 2016) to restrict the shape of the association between exposure and mortality to biologically plausible forms since the default methods like natural, restricted or penalized splines can become overly wiggly. The SCHIF permits various nonlinear shapes, including supralinear, nearlinear, and sublinear forms. Thereby, several flexible S-shaped functions are compared and the optimal model (best model fit based on the largest log-likelihood value) as well as an ensemble model (average of all models weighted by the log-likelihood values) are determined. Uncertainty estimates of the ensemble model predictions are obtained by bootstrap methods which incorporate both sampling and model shape uncertainty. The confidence bands are narrowest at the low end of the exposure since the lowest concentration value is chosen as reference by default.

Though we consider the non-parametric nature of splines more advantageous for assessing the shape of the concentration-response function than the SCHIF approach that borrows information from assumptions about the shape of the function, we performed the SCHIF method to compare our results with recent studies from Canada (Bai et al. 2019, Pinault et al. 2017). Furthermore, for health impact assessment, the biologically more plausible SCHIF functions are more attractive than splines. The uncertainty of the prediction differs considerably between the spline and SCHIF method due to differences in the general setup and related assumptions. Since the lowest concentration value is chosen as reference for the SCHIF plots, the confidence bands get wider with increasing pollutant concentrations. The splines, however, incorporate the standard error of the estimated function in the curve uncertainty, which is wider where data are fewer and thus, show largest uncertainty at the tails of the distribution. We therefore focused our comparison on the 5th and 95th percentiles of the exposure distribution.

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Supplementary Methods M5. Time-varying exposure analyses

We used time varying exposure analyses and the concentration back extrapolated to the year of recruitment as alternative exposure variables. Residential history was incorporated in the time varying exposure analyses, such that both changes in air pollution spatial patterns and moving residential address were accounted for. The baseline exposure was assessed at the residential address at baseline, as was the 2010 exposure. Back-extrapolation was performed with both the difference and ratio method (see Supplementary Methods M3. Detailed exposure assessment and procedure for back-extrapolation). The procedure scales back the 2010 exposure surface, with time trends represented at a large spatial scale, typically one or a few distinct values per cohort. The trend correction was allowed to differ across cohorts.For cohorts with complete residential history (CEANS, DCH, EPIC-NL), we investigated time-varying exposure analyses including residential mobility by linking back-extrapolated annual average concentrations per year to each address from baseline to censoring. We therefore restructured our data set and included one row for each year or address change from baseline examination until end of follow-up according to the residential history of the participants. Back-extrapolated annual average concentrations were then linked to each address from baseline to censoring. We applied time-dependent Cox proportional hazards models additionally incorporating a 1-year or 5-year strata of follow-up time to account for time trends in incidence. In addition to the linear time-varying exposure analyses, we also specified spline functions to test the sensitivity of our findings with respect to the level at which associations are observed. We used natural splines with three degrees of freedom, the ratio back-extrapolation and 1-year strata to adjust for time trends.

Supplementary Methods M6. Noise assessment

Road traffic noise levels (Lden: day-evening-night equivalent level) at the baseline address were assessed locally by using noise modelling according to the EU noise directive 2002/49/EC for the most exposed façade of dwellings. National calculation methods were used in the study areas of the Danish (Nordic Prediction Method) and German cohorts, while a locally developed validated model was used for the Swedish cohorts (see table below). Noise barriers and actual or estimated building heights and terrain effects from absorption and reflection in the ground were included in the German models. To assess traffic flow, composition and speed for the full road network, different methods were applied within each study area. For motorways, actual traffic counts were used. For other roads, if counts were not available, traffic forecast models were used or flows were estimates from counts. For smaller road standard, traffic flows were used. For roads were no actual composition was known, standard distributions were used. For the majority of the roads the speed limit was used. The exposure at the most exposed façade with a resolution of 0·1 dB was obtained from grids (HNR 10x10 m) or by using an assessment point directly at this façade (CEANS, DCH, and KORA). The software used was CadnaA (HNR, KORA) and Soundplan (DCH). First order reflections were included in the calculations. In the DCH and DNC cohorts, both first and second order reflections were included.

Table M7: Overview of available noise exposure models

Cohort	Noise model	Exposures available	Years	Comments
CEANS	Local model[1] based on Nordic Prediction Method[2]	Yes	1990 onwards for road traffic (data from the years 1990, 1995, 2000, 2005 and 2010 with linear extrapolation between these years)	Separately for roads, rail, aircraft; every fifth year with interpolation in-between
DCH	Nordic Prediction Method[2]	Yes	1995	Information on road traffic noise at baseline
DNC	Nord2000[3]	Yes	1993 or 1999	Road traffic, wind turbine
EPIC-NL		No		
HNR	VBUS/RLS-90[a]	Yes	2006	Assessment for road traffic according to European Noise Directive
KORA	VBUS/RLS-90[a]	Yes	2009	Assessment for road traffic according to European Noise Directive

[a] Noise levels estimated according to the guidelines for noise protection at roads (“Richtlinien für den Lärmschutz an Straßen”, RLS-90) and interim calculation method for environmental noise at roads (“Vorläufigen Berechnungsmethode für den Umgebungslärm an Straßen”,VBUS).

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Supplementary Table S1. **Detailed description of the study population: individual baseline characteristics of six European cohorts (12 sub-cohorts).**

	CEANS				DCH	DNC		EPIC NL		HNR	KORA		
Variable	**SDPP**	**SIXTY**	**SALT**	**SNAC-K**		**1993**	**1999**	**MORGEN**	**PROSPECT**		**S3**	**S4**	**Pooled**
N of participants – pooled ELAPSE data set	7,835	4,180	6,724	3,248	56,308	19,664	8,769	20,711	16,194	4,809	4,566	4,257	157,265
N eligible for incidence analyses*	7,802	4,045	6,441	2,908	54,808	19,377	8,688	20,015	15,794	4,446	3,910	3,747	151,981
% of the original ELAPSE data set	99.6	97	96	90	97	99	99	97	98	92	86	88	97
N – main model	7,488	3,814	5,929	2,547	52,088	16,810	8,055	17,643	14,204	4,375	2,182	2,013	137,148
% of the incidence data set	96	94	92	88	95	87	93	88	90	98	56	54	90
Individual characteristics													
Marital status, %													
Single	16	5	14	17	6	11	9	25	6	6	9	8	10
Married/living with partner	84	74	68	47	72	68	76	66	77	75	82	80	72
Divorced/separated	0	16	11	14	17	12	13	8	8	10	4	7	12
Widowed	0	5	7	23	6	9	2	2	9	9	5	6	6
BMI (kg/m²), mean ± SD	26 ± 4	27 ± 4	25 ± 3	26 ± 4	26 ± 4	24 ± 3	24 ± 4	25 ± 4	26 ± 4	28 ± 5	27 ± 4	27 ± 5	26 ± 4
Underweight (< 18·5), %	1	1	2	3	1	3	2	1	1	0	1	0	1
Normal weight (18·5-24·9), %	48	36	59	44	44	69	69	50	45	27	34	32	49
Pre-obesity (25·0-29·9), %	39	45	33	41	41	23	23	38	40	46	44	44	37
Obesity (BMI ≥ 30·0), %	13	19	6	13	14	5	7	11	15	27	22	24	13
Smoking status, %													
Never	37	41	46	47	36	34	39	37	44	43	52	46	39
Former	36	38	33	38	28	28	33	28	33	33	28	31	30
Current	26	21	21	15	36	38	29	35	23	24	20	23	31
Years of smoking, mean ± SD	13 ± 13	15 ± 16	14 ± 17	16 ± 19	19 ± 17	16 ± 16	12 ± 13	13 ± 13	16 ± 17	15 ± 16	9 ± 13	11 ± 13	16 ± 16
Number of cigarettes/day, mean ± SD	8 ± 9	8 ± 9	7 ± 10	4 ± 6	10 ± 11	8 ± 9	7 ± 8	10 ± 11	6 ± 8	12 ± 16	8 ± 13	9 ± 14	9 ± 11
Education, %													
Primary school or less	31	40	26	25	15	0	0	11	22	11	14	10	14
Secondary school	38	32	36	40	63	0	0	81	74	56	72	70	51
University degree and more	30	28	37	35	22	100	100	8	4	33	14	20	34
Noise (Lden, dB; lower cut-off value 45dB), mean ± SD	46 ± 3	50 ± 6	50 ± 6	59 ± 7	58 ±7	53 ± 6	53 ± 6	*NA*	*NA*	55 ± 9	54 ± 6	54 ± 6	55 ± 7
Missing (N)	*0*	*0*	*0*	*0*	*39*	*0*	*0*	*NA*	*NA*	*30*	*1*	*6*	*31,923*

CEANS: Cardiovascular Effects of Air Pollution and Noise in Stockholm (with sub-cohorts SDPP: Stockholm Diabetes Prevention Program; SIXTY: the Stockholm 60 years old study; SALT: the Stockholm Screening Across the Lifespan Twin study and TwinGene (subset living in Stockholm); SNAC-K: the Swedish National Study on Aging and Care in Kungsholmen); DCH: Diet, Cancer and Health; DNC: Danish Nurses Cohort (with sub-cohorts 1993 and 1999); EPIC-NL: European Prospective Investigation into Cancer and Nutrition, the Netherlands (with sub-cohorts MORGEN and PROSPECT); HNR: Heinz Nixdorf Recall study; KORA: Cooperative Health Research in the Augsburg Region (with sub-cohorts S3 and S4). * Valid outcome and follow-up information, prevalent cases excluded.

Supplementary Table S2. **Two-pollutant models for stroke and coronary heart disease (CHD).** The combinations of NO_2 and BC are marked italic since most sub-cohorts indicated Spearman correlation > 0·7, thus estimates are considered only explorative.

			Single pollutant model	Two pollutant model, adjusted for			
				$PM_{2·5}$	NO_2	BC	O_3 warm
	Pollutant	**Increment**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**
Stroke	$PM_{2·5}$ (μg/m^3)	5	1·10 (1·01– 1·21)	-	0·97 (0·86– 1·09)	1·02 (0·91– 1·14)	1·09 (0·98– 1·20)
	NO_2 (μg/m^3)	10	1·08 (1·04– 1·12)	1·09 (1·03– 1·14)	-	*1·11 (1·02– 1·20)*	1·09 (1·04– 1·14)
	BC (10^{-5}/m)	0·5	1·06 (1·02– 1·10)	1·06 (1·01– 1·11)	*0·97 (0·89– 1·05)*	-	1·06 (1·02– 1·11)
	O_3 warm (μg/m^3)	10	0·96 (0·91– 1·01)	0·98 (0·92– 1·04)	1·03 (0·97– 1·10)	1.00 (0·94– 1·07)	-
CHD	$PM_{2·5}$ (μg/m^3)	5	1·02 (0·95– 1·10)	-	0·94 (0·85– 1·03)	0·98 (0·89– 1·08)	0·98 (0·90– 1·07)
	NO_2 (μg/m^3)	10	1·04 (1·01– 1·07)	1·06 (1·02– 1·10)	-	*1·09 (1·02– 1·17)*	1·02 (0·98– 1·06)
	BC (10^{-5}/m)	0·5	1·02 (0·99– 1·06)	1·03 (0·99– 1·07)	*0·94 (0·88– 1·01)*	-	1.00 (0·96– 1·04)
	O_3 warm (μg/m^3)	10	0·94 (0·90– 0·98)	0·94 (0·90– 0·98)	0·96 (0·91– 1·01)	0·94 (0·90– 0·99)	-

HR: hazard ratio; CI: confidence interval. All models adjusted for sub-cohort (strata), age (time scale), sex (strata), year of baseline visit, marital status, BMI, smoking (status, duration, intensity, intensity^2), employment status, education, and neighborhood mean income.

Supplementary Table S3. **Back-extrapolated air pollution exposure at baseline and stroke and coronary heart disease (CHD) incidence .** Back-extrapolation was performed back to the time of enrolment and based on the Danish Hemispheric Eulerian (DEHM) Model using the absolute difference and the ratio between the baseline and 2010.

			Model 3	**Back-extrapolated baseline exposure**	
				Ratio method	**Difference method**
	Pollutant	**Increment**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**
Stroke	$PM_{2·5}$ (μg/m^3)	5	1·10 (1·01– 1·21)	1·05 (1.00– 1·09)	1·04 (0·99– 1·10)
	NO_2 (μg/m^3)	10	1·08 (1·04– 1·12)	1·06 (1·03– 1·09)	1·08 (1·04– 1·12)
	BC (10^{-5}/m)	0·5	1·06 (1·02– 1·10)	1·05 (1·02– 1·08)	1·06 (1·02– 1·10)
	O_3 warm (μg/m^3)	10	0·96 (0·91– 1·01)	0·95 (0·91– 1.00)	0·95 (0·91– 1.00)
CHD	$PM_{2·5}$ (μg/m^3)	5	1·02 (0·95– 1·10)	1.00 (0·96– 1·04)	1.00 (0·96– 1·04)
	NO_2 (μg/m^3)	10	1·04 (1·01– 1·07)	1·03 (1·01– 1·05)	1·04 (1·01– 1·07)
	BC (10^{-5}/m)	0·5	1·02 (0·99– 1·06)	1·02 (1.00– 1·05)	1·02 (0·99– 1·05)
	O_3 warm (μg/m^3)	10	0·94 (0·90– 0·98)	0·94 (0·91– 0·98)	0·94 (0·91– 0·98)

HR: hazard ratio; CI: confidence interval. All models adjusted for sub-cohort (strata), age (time scale), sex (strata), year of baseline visit, marital status, BMI, smoking (status, duration, intensity, intensity^2), employment status, education, and neighborhood mean income.

Supplementary Table S4. Time-varying air pollution exposure including residential mobility among cohorts with available address history information (CEANS, DCH, EPIC_NL). Hazard ratios for associations between air pollution and stroke and coronary heart disease (CHD) incidence. Back-extrapolation was performed back to the residential history between enrolment and end-of follow-up and based on the Danish Hemispheric Eulerian (DEHM) Model using the absolute difference and the ratio between the baseline and 2010 periods.

			Main model 3	Time-varying analyses			
			Reduced data set[a]	Strata per year of follow up time to account for time trend		Strata by 5-years of follow up time to account for time trend	
			(N=101,328)	Ratio method	Difference method	Ratio method	Difference method
	Pollutant	Increment	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Stroke	$PM_{2·5}$ (μg/m^3)	5	1·08 (0·98– 1·20)	1·12 (1·03– 1·22)	1·14 (1·03– 1·26)	1·10 (1·03– 1·16)	1·09 (1·02– 1·15)
	NO_2 (μg/m^3)	10	1·08 (1·03– 1·12)	1·11 (1·07– 1·15)	1·11 (1·07– 1·16)	1·11 (1·07– 1·15)	1·12 (1·07– 1·16)
	BC (10^{-5}/m)	0·5	1·06 (1·01– 1·10)	1·11 (1·06– 1·15)	1·10 (1·05– 1·14)	1·10 (1·06– 1·15)	1·10 (1·06– 1·14)
	O_3 warm (μg/m^3)	10	0·99 (0·93– 1·05)	0·96 (0·93– 0·99)	0·96 (0·93– 0·99)	0·97 (0·94– 0·99)	0·97 (0·94– 0·99)
CHD	$PM_{2·5}$ (μg/m^3)	5	1·06 (0·96– 1·16)	1·03 (0·96– 1·11)	1·04 (0·94– 1·14)	1·04 (0·99– 1·10)	1·04 (0·99– 1·10)
	NO_2 (μg/m^3)	10	1·06 (1·02– 1·10)	1·05 (1·02– 1·08)	1·05 (1·01– 1·09)	1·05 (1·02– 1·08)	1·05 (1·01– 1·09)
	BC (10^{-5}/m)	0·5	1·03 (1·00– 1·07)	1·03 (0·99– 1·07)	1·03 (0·99– 1·07)	1·03 (0·99– 1·07)	1·03 (0·99– 1·07)
	O_3 warm (μg/m^3)	10	0·94 (0·89– 0·98)	0·97 (0·95– 0·99)	0·97 (0·95– 0·99)	0·98 (0·96– 1·01)	0·98 (0·96– 1·00)

HR: hazard ratio; CI: confidence interval. All models adjusted for sub-cohort (strata), age (time scale), sex (strata), year of baseline visit, marital status, BMI, smoking (status, duration, intensity, intensity^2), employment status, education, and neighborhood mean income.
[a] Reduced to participants with available address history information who were included in the time-varying exposure analyses.

Supplementary Table S5. **Sensitivity analysis: additional adjustment for noise.** Hazard ratios (HR) and 95%-confidence intervals (CI) for all participants (N=137,148) and reduced to participants with noise information (N=105,225) without and with adjustment for noise.

			All cohorts/participants (N=137,148)	Cohorts/participants with available noise data (N=105,225)	
			Main model	Main model	Additionally adjusted for noise
	Pollutant	**Increment**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**
Stroke	$PM_{2·5}$ (µg/m^3)	5	1·10 (1·01– 1·21)	1·12 (1·02– 1·23)	1·09 (0·99– 1·21)
	NO_2 (µg/m^3)	10	1·08 (1·04– 1·12)	1·08 (1·04– 1·12)	1·08 (1·03– 1·12)
	BC (10^{-5}/m)	0·5	1·06 (1·02– 1·10)	1·06 (1·02– 1·11)	1·05 (1·01– 1·10)
	O_3 warm (µg/m^3)	10	0·96 (0·91– 1·01)	0·95 (0·90– 1·01)	0·97 (0·91– 1·04)
CHD	$PM_{2·5}$ (µg/m^3)	5	1·02 (0·95– 1·10)	1·02 (0·94– 1·10)	1·01 (0·92– 1·10)
	NO_2 (µg/m^3)	10	1·04 (1·01– 1·07)	1·03 (0·99– 1·06)	1·03 (0·99– 1·07)
	BC (10^{-5}/m)	0·5	1·02 (0·99– 1·06)	1·02 (0·99– 1·06)	1·02 (0·98– 1·06)
	O_3 warm (µg/m^3)	10	0·94 (0·90– 0·98)	0·94 (0·89– 0·99)	0·94 (0·89– 1.00)

All models adjusted for sub-cohort (strata), age (time scale), sex (strata), year of baseline visit, marital status, BMI, smoking (status, duration, intensity, intensity^2), employment status, education, and neighborhood mean income.

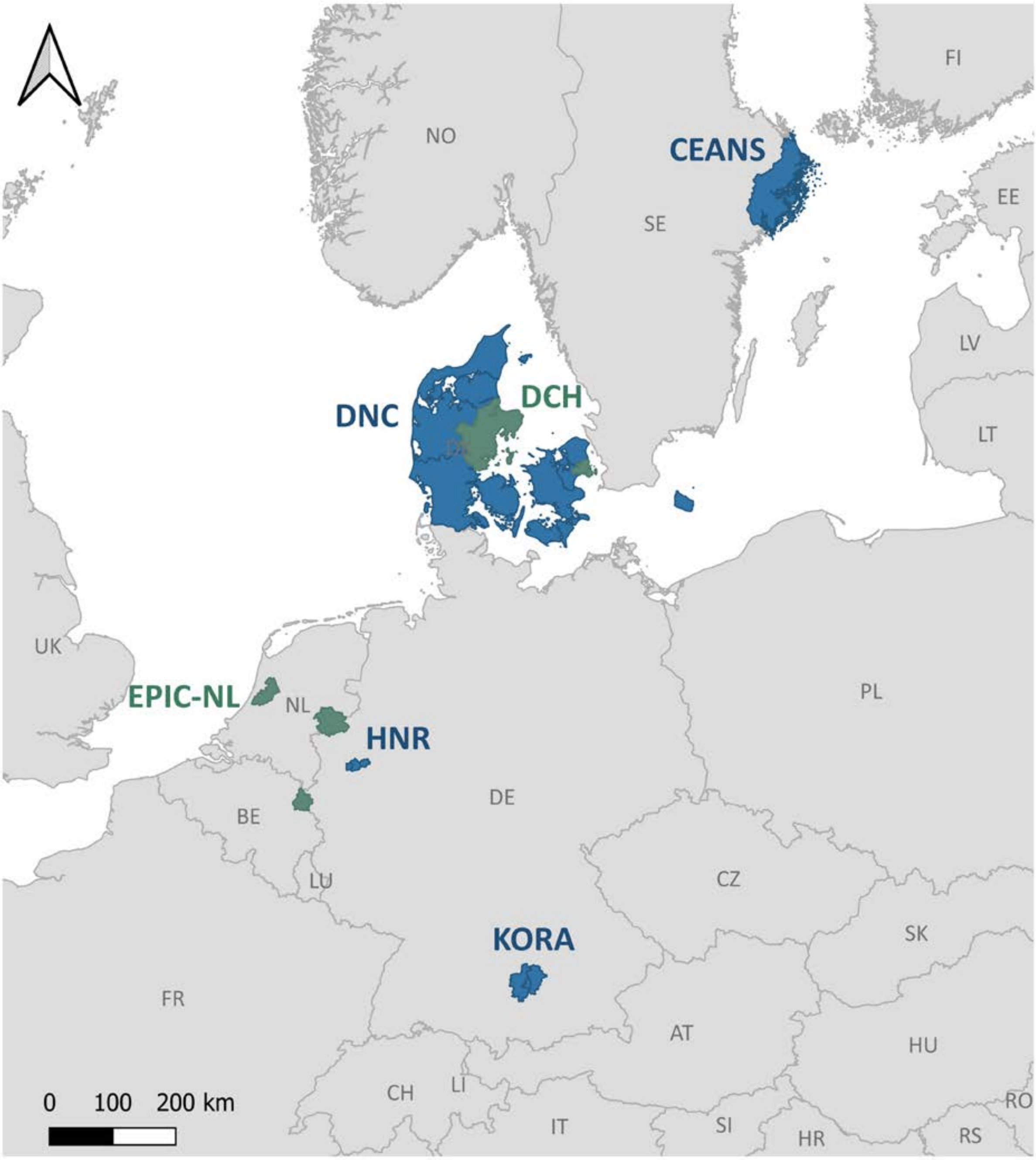
Supplementary Table S6. **Sensitivity analysis: Hazard ratios (HR) and 95%-confidence intervals (CI) for all participants (N=137,148) with and without adjustment for BMI.**

			Main model[a]	Without adjustment for BMI[b]
	Pollutant	**Increment**	**HR (95% CI)**	**HR (95% CI)**
Stroke	$PM_{2·5}$ (μg/m^3)	5	1·10 (1·01– 1·21)	1·11 (1·01– 1·21)
	NO_2 (μg/m^3)	10	1·08 (1·04– 1·12)	1·08 (1·04– 1·12)
	BC (10^{-5}/m)	0·5	1·06 (1·02– 1·10)	1·06 (1·02– 1·10)
	O_3 warm (μg/m^3)	10	0·96 (0·91– 1·01)	0·96 (0·91– 1·01)
CHD	$PM_{2·5}$ (μg/m^3)	5	1·02 (0·95– 1·10)	1·03 (0·95– 1·11)
	NO_2 (μg/m^3)	10	1·04 (1·01– 1·07)	1·04 (1·01– 1·07)
	BC (10^{-5}/m)	0·5	1·02 (0·99– 1·06)	1·02 (0·99– 1·06)
	O_3 warm (μg/m^3)	10	0·94 (0·90– 0·98)	0·94 (0·90– 0·98)

[a]Adjusted for sub-cohort (strata), age (time scale), sex (strata), year of baseline visit, marital status, BMI, smoking (status, duration, intensity, intensity^2), employment status, education, and neighborhood mean income.

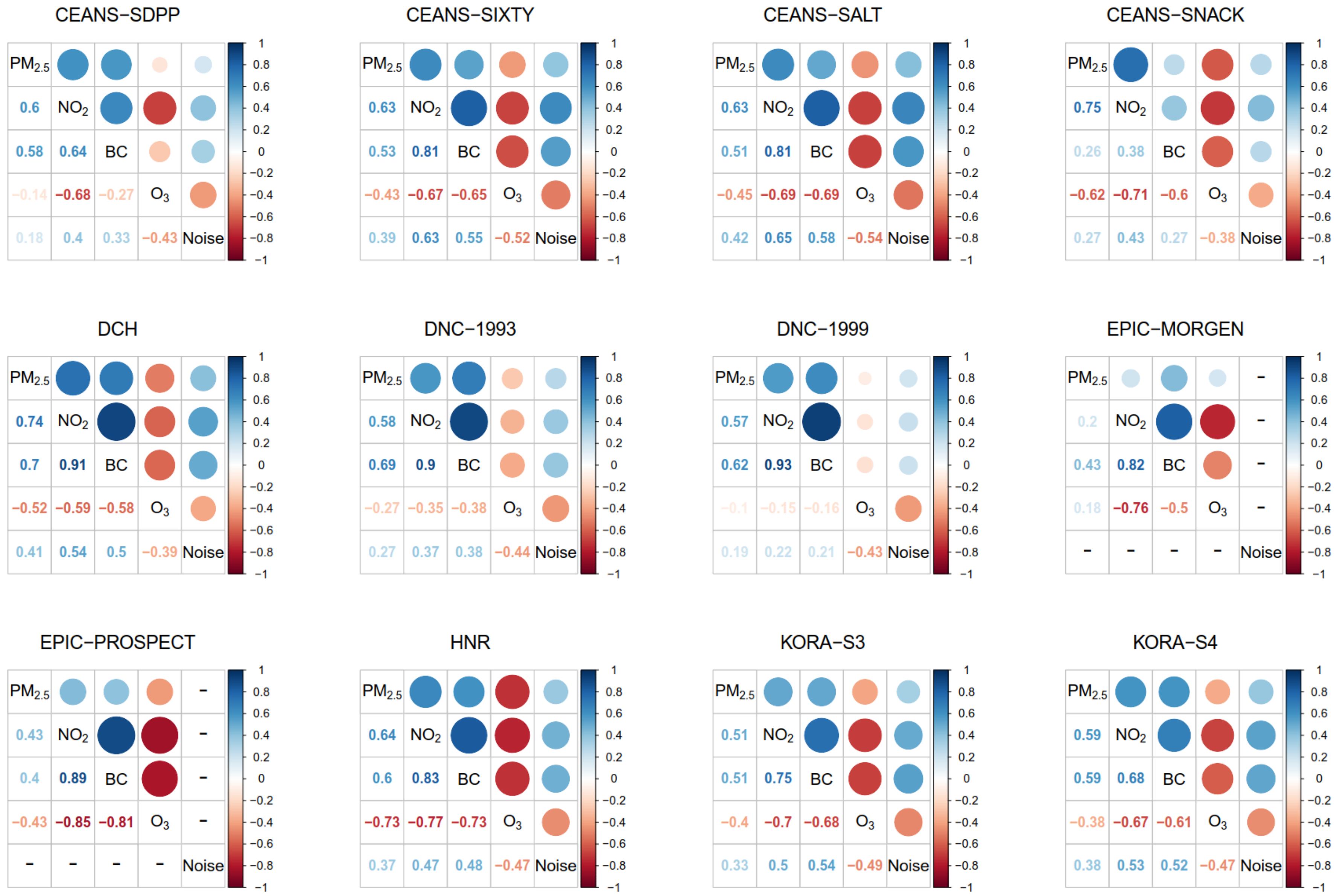
[b]Adjusted for sub-cohort (strata), age (time scale), sex (strata), year of baseline visit, marital status, smoking (status, duration, intensity, intensity^2), employment status, education, and neighborhood mean income.

Supplementary Figure S1. Map of the study areas.



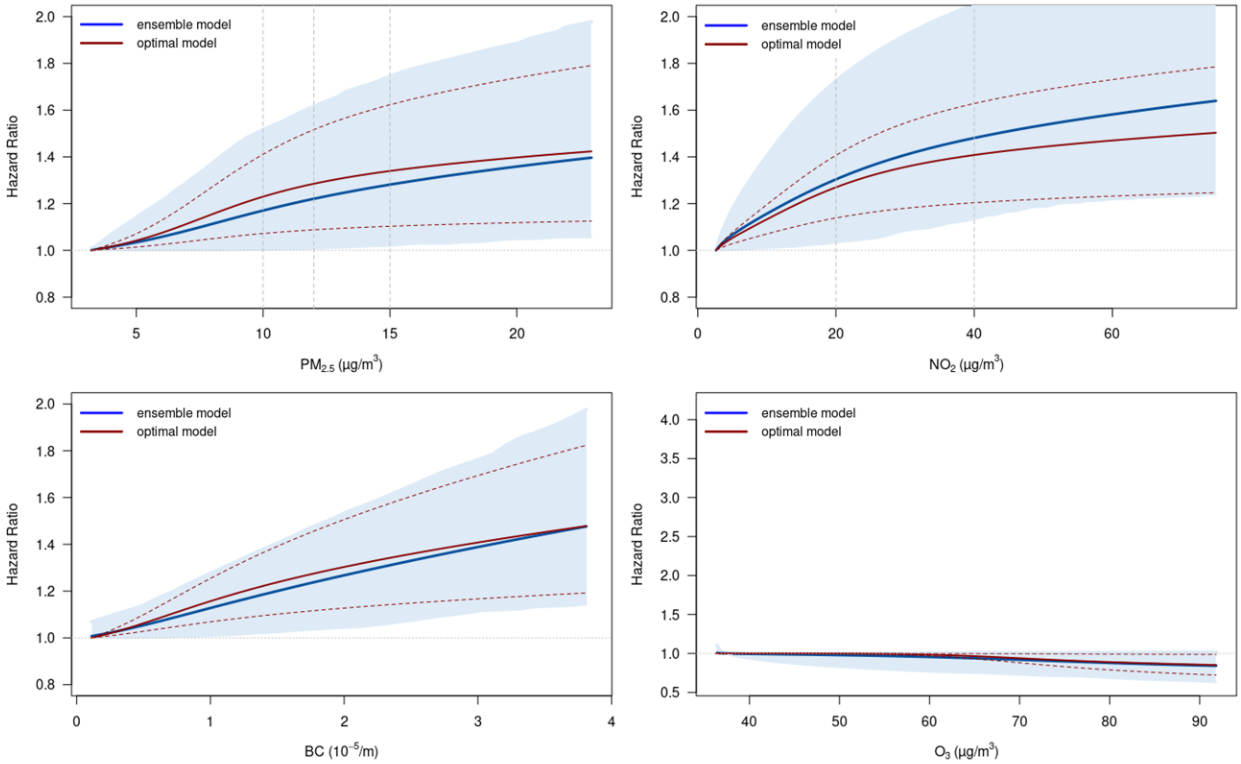
CEANS: Cardiovascular Effects of Air Pollution and Noise in Stockholm; DCH: Diet, Cancer and Health; DNC: Danish Nurses Cohort; EPIC-NL: European Prospective Investigation into Cancer and Nutrition, the Netherlands; HNR: Heinz Nixdorf Recall study; KORA: Cooperative Health Research in the Augsburg Region.

Supplementary Figure S2. Spearman correlation coefficients per sub-cohort. $PM_{2.5}$: particulate matter ≤2·5 µm; NO_2: nitrogen dioxide; BC: black carbon; O_3: warm season ozone.

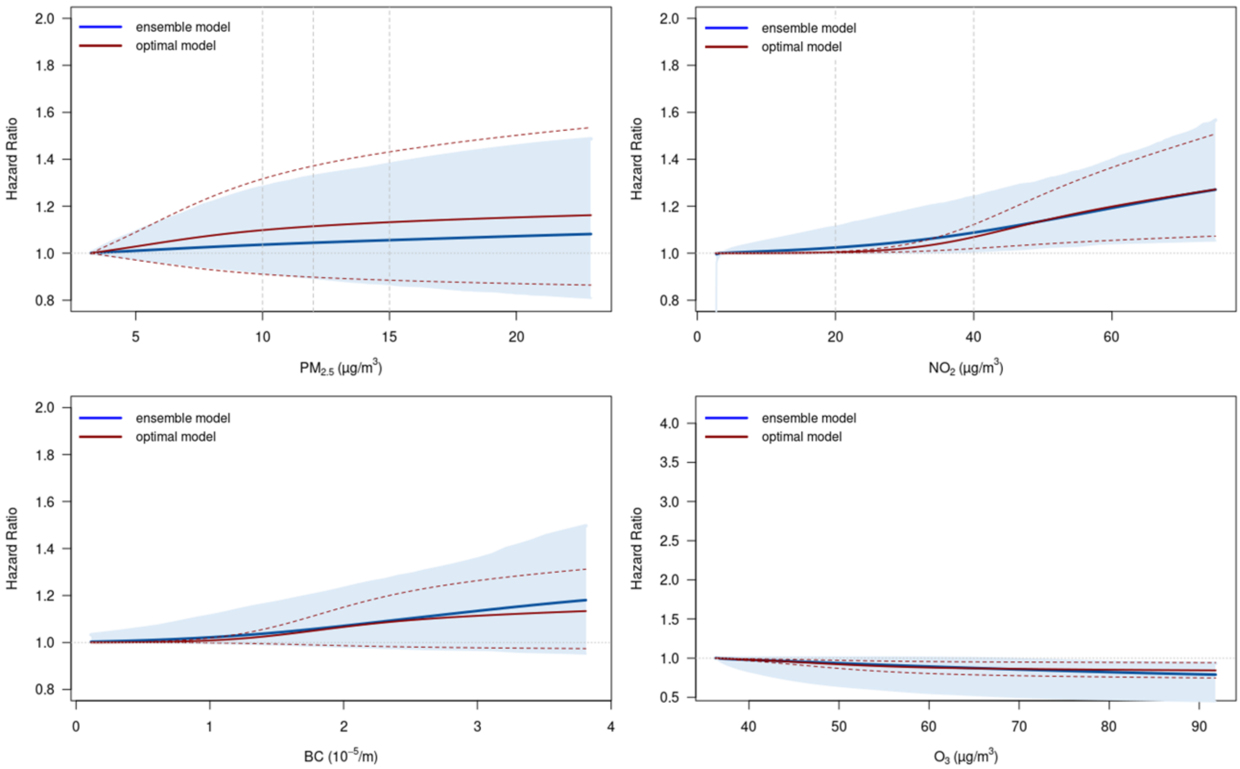


Supplementary Figure S3. Shape-Constrained Health Impact Functions for stroke (A) and coronary heart disease (B). Optimal hazard function (red solid line) with uncertainty bounds (dashed red lines) and ensemble hazard function (blue solid line) with uncertainty bounds (blue-shaded area). All models adjusted for sub-cohort (strata), age (time scale), sex (strata), year of baseline visit, marital status, BMI, smoking (status, duration, intensity, intensity²), employment status, education, and neighborhood mean income. Grey dotted vertical lines indicate limit and guideline values. HR=1 for minimum pollution exposure.

A: Stroke

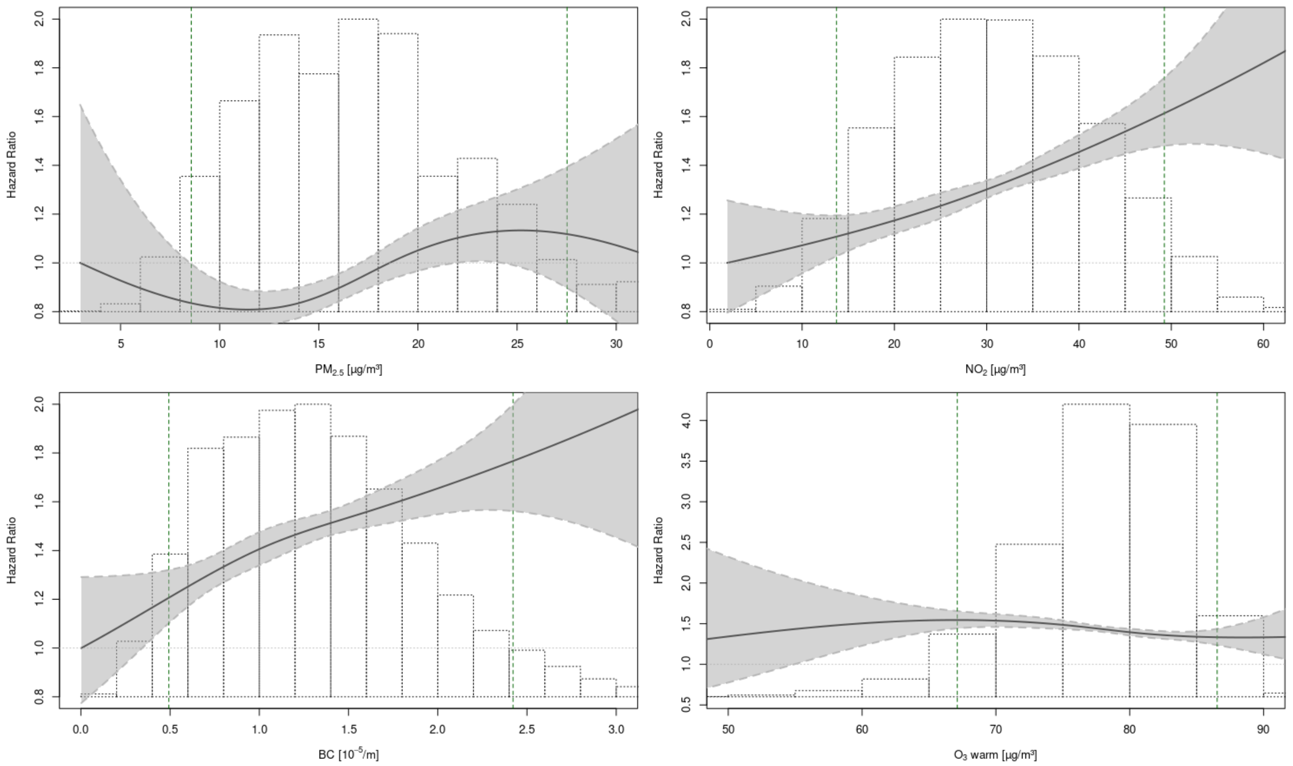


B: Coronary heart disease

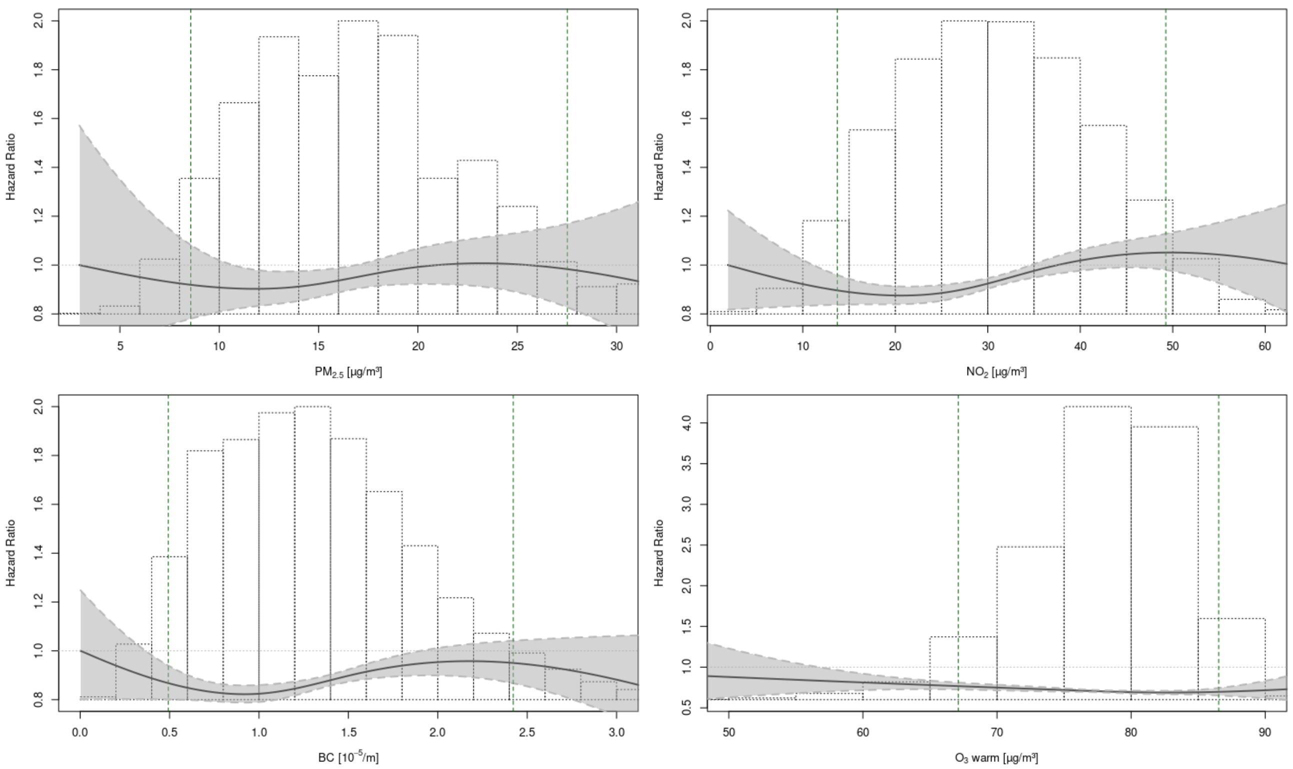


Supplementary Figure S4. Time-varying exposure analyses using back-extrapolated concentrations: Natural cubic splines with three degrees of freedom (solid line) with 95% confidence bands (dark shaded) for stroke (A) and coronary heart disease (B). All models adjusted for sub-cohort (strata), age (time scale), sex (strata), year of baseline visit, marital status, BMI, smoking (status, duration, intensity, intensity²), employment status, education, and neighborhood mean income. Light grey bars indicate the distribution of the air pollutant and dashed vertical lines the 5th and 95th percentiles. Hazard Ratios were set to 1 for minimum pollution exposure.

A: Stroke

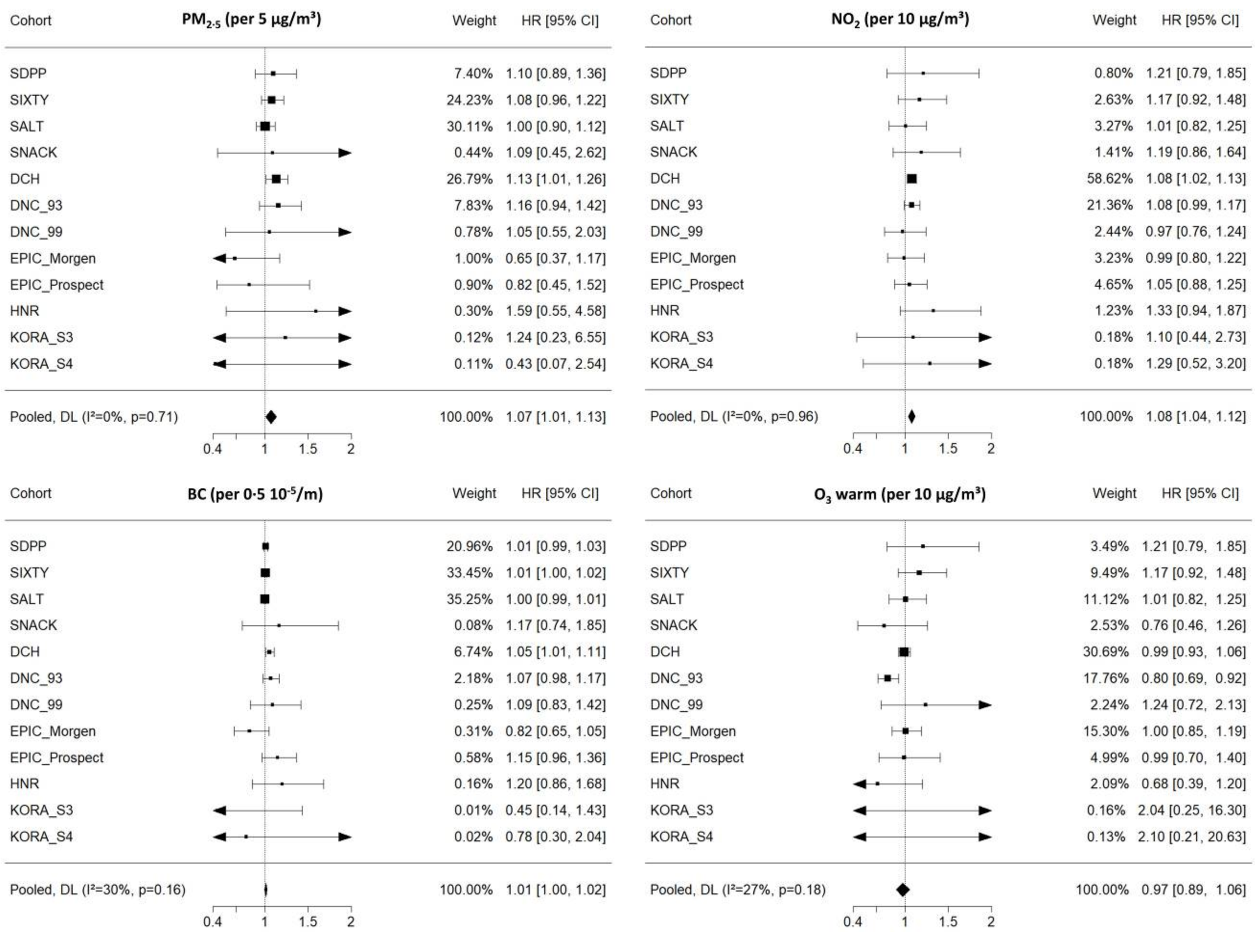


B: Coronary heart disease

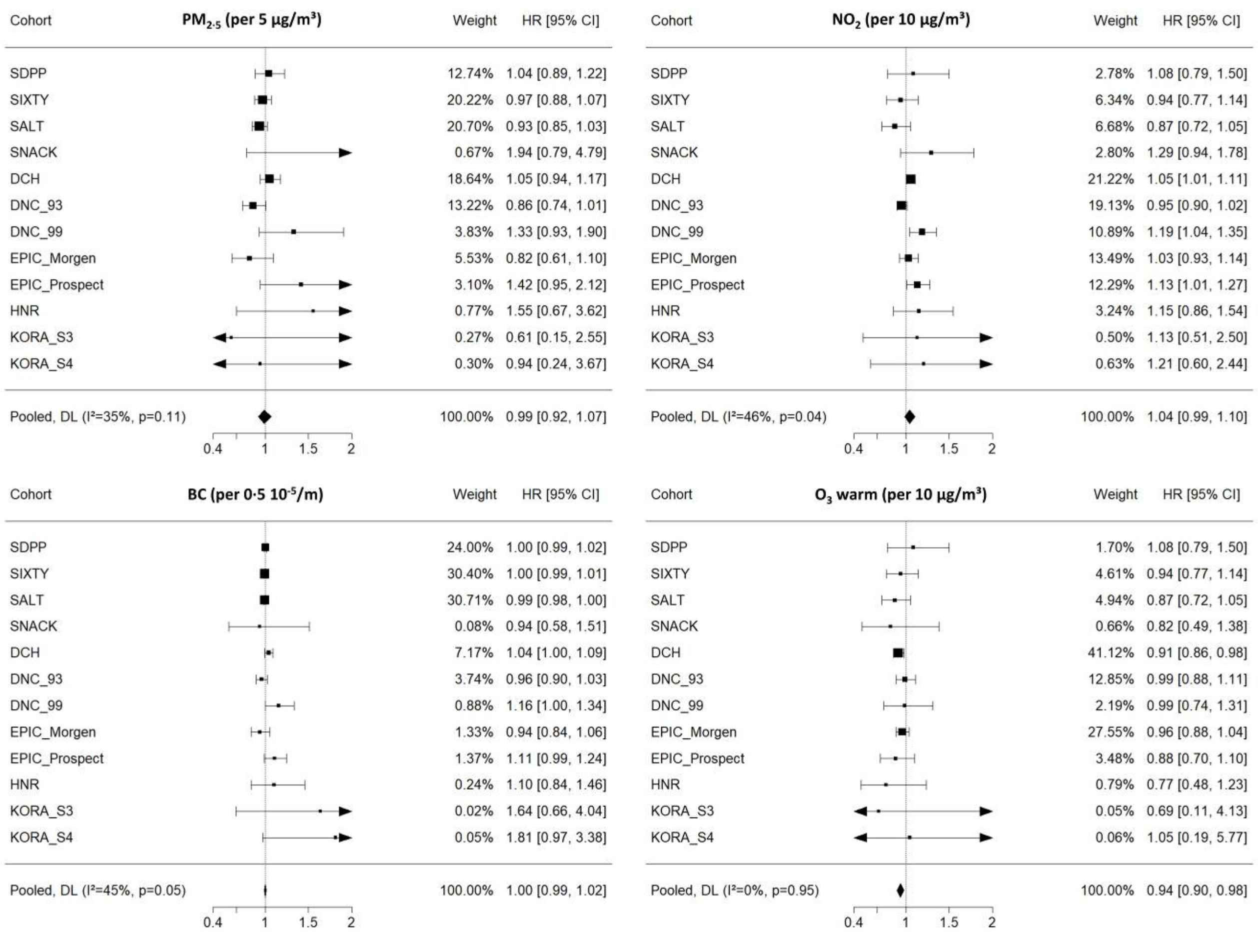


Supplementary Figure S5. Meta-analysis: Cohort-specific and pooled hazard ratios (HR) and 95% confidence intervals (CI) per fixed increase of air pollutants on incidence of stroke (A) and coronary heart disease (B). All models adjusted for sub-cohort (strata), age (time scale), sex (strata), year of baseline visit, marital status, BMI, smoking (status, duration, intensity, intensity²), employment status, education, and neighborhood mean income. DL: DerSimonian & Laird, EB: Empirical Bayes, I²: I² statistic, p: P value of test for heterogeneity.

A: Stroke

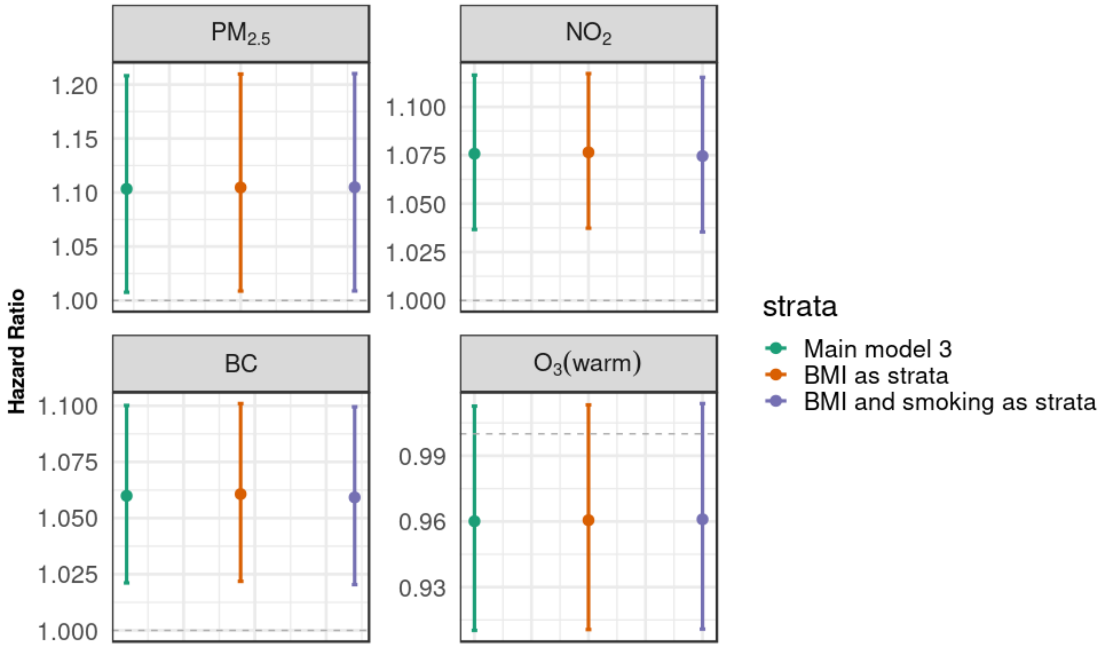


B: Coronary heart disease

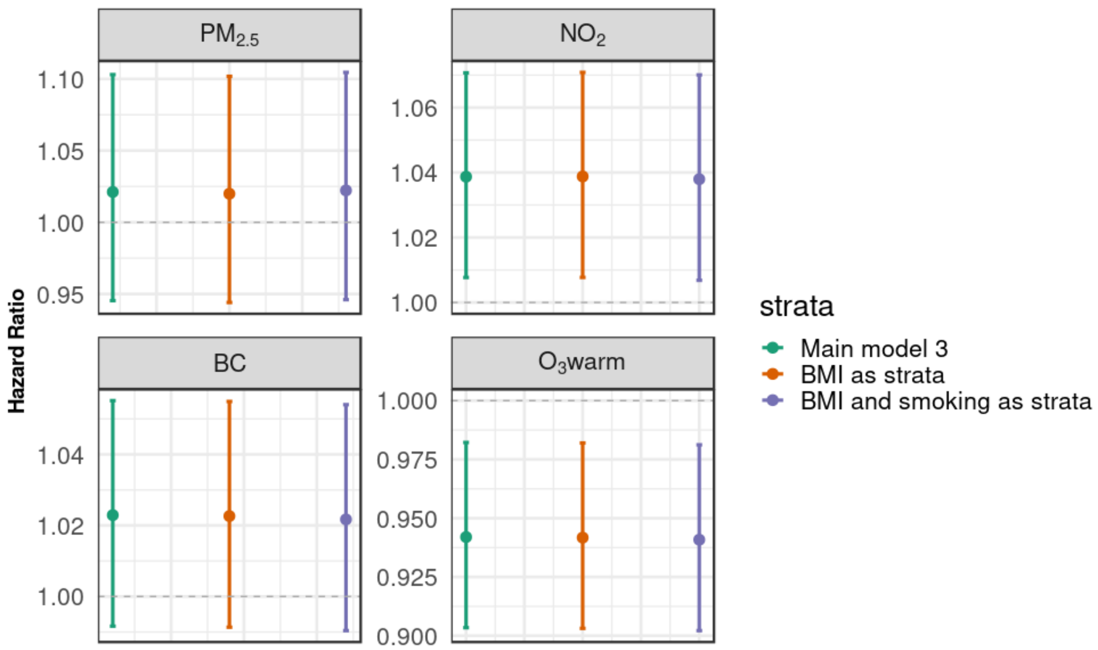


Supplementary Figure S6. Sensitivity analysis: Inclusion of variables that did not fulfill the proportional hazards assumption as strata. Hazard ratios (HR) and 95%-confidence intervals (CI). Main model 3 adjusted for sub-cohort (strata), age (time scale), sex (strata), year of baseline visit, marital status, BMI, smoking (status, duration, intensity, intensity²), employment status, education, and neighborhood mean income.

A: Stroke



B: Coronary heart disease



Remark: We tested all covariates jointly and selected the covariate with lowest p-value (BMI) among those covariates indicating violation of the proportional hazards assumption. We then run the model with strata for BMI and tested again all remaining covariates. Since smoking still indicated violation, we rerun the model with strata for BMI and strata for smoking for which the test indicated no further violation. Following this stratey, we did not investigate smoking as only strata but do not expect substantial differences in effect estimates since all estimates (main model 3, BMI as strata, BMI and smoking as strata) were almost identical.