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Supplementary appendix

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APPENDIX

Long-term Exposure to Low Ambient Air Pollution Concentrations and Mortality among 28 Million Subjects – Results from seven European large cohorts within the ELAPSE Project

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1. Extended data

1.1 The cohorts

1.1.1 Belgian cohort

The Belgian 2001 Census cohort is based on the entire Belgian population officially residing in Belgium in 2001. Emigration and mortality follow-up data is available for the period from 01/10/2001-31/12/2011 (10.25 years). Data were made available by the Belgian statistical office (Statbel). Additionally, geocoding of the residential addresses at baseline, and linkage of air pollution exposure data was performed by Statbel. Geographical coverage was almost complete with 98.7% of individuals included. Available individual covariates at baseline are: age (birth date), sex, marital status, country of origin, education level, occupational status, and residential history. Available area-level SES variables consisted of mean income, unemployment rate, low education level, and ethnicity. Area-level SES variables were available at two different spatial levels: neighborhood (i.e. sections; n=6344) and region (i.e. arrondissements NUTS 3; n=43).

1.1.2 Danish cohort

The Danish cohort consists of 3,083,235 Danish adults aged ≥30 years that were followed-up from 01/01/2000 until 12/31/2015; study inclusion required residency in Denmark for at least one year prior to baseline. The data was assembled and stored on Statistics Denmark secure server. Individual-level demographics (date of birth, sex, country of origin, household income, employment status) from 2000, and area-level socioeconomic status from 2001 (mean household income, percentage of unemployed and low education level at the parish and region levels) were obtained from the population registries. Natural cause and cause-specific mortality were obtained from the causes of death register. The population and causes of death registers from 2000 were also obtained for calculating age-standardized municipality-level mortality rates from lung cancer, chronic obstructive pulmonary disease, and diabetes. Additionally, residential addresses at baseline were geocoded and linked to air pollution exposure data. Data access for this study was granted by Danish Data Protection Agency, the Danish Health Data Authority and Statistics Denmark. Because the study was based exclusively on registry data, according to Danish legislation and GDPR, informed consent from cohort members was not required.

1.1.3 Dutch cohort

The Dutch Environmental Longitudinal Study (DUELS) is described in detail by Fischer et al. (2015).[1] Briefly, population statistics based on digital municipal registers are combined by Statistics Netherlands into a longitudinal file for each individual registered in the municipal registration. Changes in demographic attributes (e.g., death, address, marital status, emigration, region of origin) are updated yearly. In these files, the individual identification number is replaced by an encrypted unique identification number. This identification number is used to enrich the individual files with information from other central data sources available at Statistics Netherlands, including data from tax records. In the paper by Fischer et al. (2015), we selected all Dutch inhabitants of ≥30 years of age on 1/1/2004, living at the same residential address since 1/1/1999. For the ELAPSE study, we shifted the baseline to 1/1/2008 and follow-up to 1/1/2013 (i.e., 5 years). Individual-level data are available on age, sex, country of origin, marital status and household income. Area-level data are available on income, unemployment rate, ethnicity and socioeconomic score, at both regional (COROP areas, n=40) and neighborhood ("wijk", n~2700) level.

1.1.4 English cohort

The English CPRD cohort is constructed from data provided by the Clinical Practice Research Datalink (https://www.cprd.com). CPRD is a large, validated, and nationally representative database containing anonymized patient data from UK primary care. It includes a full longitudinal medical record for each patient consulting their family practitioner including information on diagnoses made within the practice. Where patient consent is given, the data are linked to death registrations and hospital admissions. Access to data in CPRD for the ELAPSE study requires three separate, consecutive approvals covering the legal basis for the linkage of primary care records to air pollution data; the scientific basis for the project including feasibility, quality and public health value; and the integrity, security and management (including linkage) of the data. The first application, to the Confidential Advisory Group, is the responsibility of CPRD, as is the application to NHS Digital (formerly HSCIC) for the actual linkage. The application for scientific approval (ISAC) is made by St George's, University of London. Individual-level data are available on age, sex, smoking status and body mass index. Area-level data are available on a composite index of socioeconomic score at regional (Strategic Health Authority) scale.

1.1.5 Norwegian cohort

NORCOHORT is the national administrative cohort of Norway. To allow the creation of the cohort, approvals from the Regional Committee for Medical and Health Research Ethics were obtained, and each registry was applied for permission to link their data to the cohort population for use of their data in ELAPSE. Furthermore, a Data Protection Impact Assessment (DPIA) was made and approved by the Data Protection Officer at the Norwegian Institute of Public Health. First, Statistics Norway draw the NORCOHORT population using the National Population Registry. The cohort consists of all residents in Norway with Norwegian citizenship being 30 years or older per 1.1.2001, including about 2.6 mill individuals. Using the personal identification number, the NORCOHORT subjects were linked to several registries; the Cancer Registry of Norway, the Norwegian Cause of Death Registry, the Cardiovascular Disease in Norway – CVDNOR – project, the Norwegian Patient Registry (NPR), the Norway Control and Payment of Health Reimbursement (KUHR), and from Statistics Norway; address history, urbanity, death and emigration, demographic, SES and noise data. The follow-up period for mortality is from 2001 to 2016. Furthermore, the CONOR cohort including lifestyle data was also linked to the NORCOHORT population. The NORCOHORT data is stored and handled in the secure Services for Sensitive Data (TSD) server based at the University of Oslo. Individual-level data are available on age, sex, marital status, family background, educational level, occupational status and household income (in categories). Regional (county, n=19) and neighborhood ("delområde", n=1,543) level data are available on income, education, unemployment, rent housing, non-western background, apartment building residence and single parent rates.

1.1.6 Rome cohort

The Rome Longitudinal Study (RoLS) is described in detail by Cesaroni et al. (2013).[2] Briefly, it includes 30+ year old subjects who filled in the Census questionnaire and were resident in Rome at 20 October 2001 (census reference day). They were identified and followed up until 2015 using the Health Information Systems of the Lazio region. The cohort is part of the National Statistical Program for the years 2017-2019 and was approved by the Italian Data Protection Authority. Individual records were linked to mortality and hospitalizations. Residential addresses were geocoded for all cohort members. Individual-level data are available on age, sex, marital status, educational level, occupational status and place of birth. Neighbourhood-level (census tract or district) data are available on income, education, unemployment rate and socioeconomic status. Regional-level data were not necessary for the Rome study area.

1.1.7 Swiss cohort

The Swiss National Cohort (SNC) is a national longitudinal research platform linking census data with birth, mortality, and emigration data. The SNC was approved by the Ethics Committees of the Cantons of Zurich and Bern. Due to mandatory participation, nearly all persons residing in Switzerland at the time of the 1990 and 2000 censuses are represented; an estimated 98.6% residents participated in 2000. For each person, the SNC contains an individual (e.g., sex, date of birth, occupation), household (e.g., type of household, socio-economic position (SEP)), and building (e.g., type of building, number of floors, geographical coordinate) record. Prior to 2010 the SNC was based on a probabilistic linkage. In 2010, Switzerland replaced the classic door-to-door census system with the registry-based census repeated each year. As such, a deterministic linkage with a unique pseudo-ID (SNC-ID), based on the social security number but cannot be traced back to it, is now used. In this new framework, data on education, occupation, employment or religion is only collected in an annual structural enquiry of a random sample of about 250,000 people per year. Swiss TPH received the latest SNC data (for 1990-2014) in October 2017 with all the necessary permissions to conduct analyses.

1.2 The surveys (for indirect adjustment of smoking and body mass index)

In each of the study areas (with the exception of UK, which had individual smoking and BMI data) a survey was available to indirectly adjust the association between air pollutants and cause-specific mortality for smoking and body mass index in the large cohorts. Individual surveys are reported in Tables S1 through S6 and compared with the corresponding data from the seven administrative cohorts.

Table S1. Exposure and covariate distributions in the main cohort and survey used for indirect adjustment of smoking and BMI in Belgium

Covariate		**Cohort (N=5,474,548)**		**Survey* (N = 5,886)**	
		mean	**sd**	**mean**	**sd**
NO_2	*µg/m³*	30.4	7.3	31.2	8.5
$PM_{2.5}$	*µg/m³*	18.6	1.6	18.3	2.1
BC	*$10^{-5}m^{-1}$*	1.8	0.3	1.8	0.4
O_3	*µg/m³*	77.0	4.6	77.5	5.0
Age (baseline)	*yr*	52.6	15.2	52.8	15.2
Neigh. mean inc. 2011	*€*	29,514	5,530	28,966	5,832
Regional mean income 2011	*€*	30,134	2,879	29,270	3,043
Neigh. unempl. rate 2011	*%*	8.0	6.0	0.1	0.1
Regional unempl. rate 2011	*%*	8.0	5.0	0.1	0.1
Neigh. education 2011	*% low*	16.0	5.0	0.2	0.1
Regional education 2011	*% low*	16.0	2.0	0.2	0.0
Neigh. ethnicity 2001	*% ethnic*	5.4	9.2	7.8	12.0
Regional ethnicity 2001	*% ethnic*	5.9	6.4	9.6	9.5
		N	**%**	**N**	**%**
Sex	*Female*	2,704,580	49.4	3,033	51.5
	Male	2,769,968	50.6	2,853	48.5
Education level	*Low*	1,301,659	23.8	1,237	21.0
	Medium	2,839,960	51.9	2,998	50.9
	High	1,332,929	24.3	1,651	28.0
Occupation status	*Employed*	2,919,408	53.3	3,107	52.8
	Unemployed	276,948	5.1	340	5.8
	Homemaker	463,245	8.5	580	9.9
	Retired	1,814,947	33.2	1,859	31.6
Country of origin	*Local*	5,302,118	96.9	5,575	94.7
	Other	172,430	3.1	311	5.3

* Population representative Health Interview Survey 2001

Table S2. Exposure and covariate distributions in the main cohort and survey used for indirect adjustment of smoking and BMI in Denmark

Covariate		**Cohort (N=3,083,235)**		**Survey* (N = 139,203)**	
		mean	**sd**	**mean**	**sd**
NO_2	$\mu g/m^3$	20.3	7.9	19.1	7.6
$PM_{2.5}$	$\mu g/m^3$	12.4	1.6	12.2	1.6
BC	$10^{-5}m^{-1}$	1.0	0.4	1.0	0.3
O_3	$\mu g/m^3$	80.2	4.3	81.0	3.8
Age (baseline)	*yr*	53.0	15.1	55.6	14.0
Household income **	*€*	162,308	167,476	237,486	110,793
Neigh. mean inc. 2001 **	*€*	165,011	27,081	230,594	40,353
Regional mean income 2001 **	*€*	165,459	7,212	228,197	12,093
Neigh. unempl. rate 2001 **	*%*	1.94	0.68	1.48	0.59
Regional unempl. rate 2001 **	*%*	1.96	0.20	1.54	0.17
Neigh. education 2001 **	*% low*	32.67	8.85	28.54	8.33
Regional education 2001 **	*% low*	32.59	4.25	28.07	4.03
		N	**%**	**N**	**%**
Sex	*Female*	1,594,177	51.7	74,511	53.5
	Male	1,489,058	48.3	64,692	46.5
Income (deciles)	*1 (lowest)*	278,012	9.0	13,134	9.4
	2	298,060	9.7	13,123	9.4
	3	301,295	9.8	13,650	9.8
	4	307,172	10.0	13,886	10.0
	5	311,337	10.1	14,149	10.2
	6	314,620	10.2	14,162	10.2
	7	316,456	10.3	14,219	10.2
	8	318,085	10.3	14,201	10.2
	9	319,513	10.4	14,342	10.3
	10 (highest)	318,685	10.3	14,337	10.3
Occupational status	*Unemployed*	78,924	2.6	1,463	1.1
	Retired/student/other/cash asst./sick	1,162,463	37.7	51,296	36.8
	Employed	1,841,848	59.7	86,444	62.1
Country of origin	*Denmark*	2,907,280	94.3	132,096	94.9
	Western country	78,050	2.5	3,614	2.6
	Non-western country	97,905	3.2	3,493	2.5

* Danish National Survey, 2010 & 2013 ~160,000 subjects

** Area level SES estimates for survey sample are derived from the 2010 Danish population registries

Table S3. Exposure and covariate distributions in the main cohort and survey used for indirect adjustment of smoking and BMI in the Netherlands

Covariate		**Cohort (N=10,465,727)**		**Survey* (N = 40,016)**	
		mean	**sd**	**mean**	**sd**
NO_2	*µg/m³*	31.4	7.1	31.7	6.4
$PM_{2.5}$	*µg/m³*	16.3	1.4	16.5	1.3
BC	*$10^{-5}m^{-1}$*	1.6	0.3	1.6	0.3
O_3	*µg/m³*	74.8	5.9	74.8	5.6
Age (baseline)	*yr*	53.6	15.1	53.6	14.7
		N	**%**	**N**	**%**
Sex	*Female*	5,373,585	51.3	20,542	51.3
	Male	5,092,142	48.7	19,474	48.7
Origin	*lev. 1*	137,723	1.3	468	1.2
	lev. 2	171,112	1.6	576	1.4
	lev. 3	182,535	1.7	694	1.7
	lev. 4	58,292	0.6	255	0.6
	lev. 5	256,375	2.4	1,100	2.7
	lev. 6	994,398	9.5	3,803	9.5
	lev. 7	8,665,292	82.8	33,120	82.8
Marital status	*Single*	1,978,248	18.9	7,564	18.9
	Married	6,599,500	63.1	25,228	63.0
	Divorced	1,053,822	10.1	4,033	10.1
	Widowed	834,157	8.0	3,191	8.0
Income (percentiles)	*<1 (lowest)*	70,825	0.7	250	0.6
	1-5	155,782	1.5	523	1.3
	5-10	333,094	3.2	1,147	2.9
	10-25	1,297,705	12.4	5,183	13.0
	25-50	2,562,912	24.5	9,795	24.5
	50-75	2,861,283	27.3	10,944	27.3
	75-90	1,873,866	17.9	7,211	18.0
	90-95	650,850	6.2	2,518	6.3
	95-99	526,815	5.0	2,004	5.0
	>99 (highest)	132,595	1.3	441	1.1

* Randomly stratified sample of the Public Health Monitor 2012 (n=387,195), and therefore made similar to the cohort with regard to most individual-level characteristics

Table S4. Exposure and covariate distributions in the main cohort and survey* used for indirect adjustment of smoking and BMI in Norway

Covariate		**Cohort (N=2,309,001)**		**Survey* (N = 40,000)**	
		mean	**sd**	**mean**	**sd**
NO_2	$\mu g/m^3$	15.3	7.8	14.9	9.2
$PM_{2.5}$	$\mu g/m^3$	8.3	2.6	7.5	2.8
BC	$10^{-5}m^{-1}$	0.5	0.4	0.4	0.5
O_3	$\mu g/m^3$	74.5	3.9	73.8	3.9
Age (baseline)	*yr*	53.9	15.9	53.2	14.6
Neigh.** income 2001	*% low*	5.1	2.4	5.4	2.5
Regional** income 2001	*% low*	5.0	1.2	5.5	1.5
Neigh. ** unempl. rate 2001	*%*	1.6	0.8	1.8	0.8
Regional** unempl. rate 2001	*%*	1.6	0.4	1.8	0.3
Neigh. ** education 2011	*% low*	24.7	7.7	23.8	7.7
Regional** education 2011	*% low*	24.8	3.3	23.4	2.9
		N	**%**	**N**	**%**
Sex	*Female*	1,175,702	50.9	20,031	50.0
	Male	1,133,299	49.1	19.969	50.0
Education level	*Low*	720,257	31.2	10,454	26.1
	Medium	1,057,520	45.8	19,146	47.9
	High	531,224	23.0	10,400	26.0
Occupation status	*Employed*	1,519,637	65.8	27,676	69.2
	Unemployed	27,381	1.2	462	1.2
	Retired	761,983	33.0	11,862	29.7
Marital status	*Single*	411,200	17.8	6,891	17.2
	Married	1,369,694	59.3	25,422	63.6
	Divorced	283,817	12.3	4,422	11.1
	Widowed	244,290	10.6	3,265	8.2
Income	*Low*	538,749	23.3	8,402	21.0
	Medium-low	569,946	24.7	10,795	27.0
	Medium-high	583,177	25.3	11,068	27.7
	High	617,129	26.7	9,735	24.3

* The survey is a sample of the Norwegian CONOR cohort, stratified by county.

** Neighborhood is the Norwegian “delområde”, the area unit between “grunnkrets” (smallest area unit), and municipality. Regional level represents each county.

Table S5. Exposure and covariate distributions in the main cohort and survey used for indirect adjustment of smoking and BMI in Rome (Italy)

Covariate		**Cohort (N=1,263,712)**		**Survey* (N = 7,838)**	
		mean	**sd**	**mean**	**sd**
NO_2	*$\mu g/m^3$*	32.9	6.1	31.7	6.5
$PM_{2.5}$	*$\mu g/m^3$*	16.7	0.9	16.6	0.9
BC	*$10^{-5}m^{-1}$*	2.2	0.3	2.2	0.3
O_3	*$\mu g/m^3$*	94.6	3.1	95.1	3.1
Age (baseline)	*yr*	55.1	15.4	47.1	6.0
Unemploy. rate (neigh. 2001)	*%*	14.9	4.0	15.2	4.2
Education level (neigh. 2001)	*% very low*	25.2	6.6	6.8	12.7
	% high	13.2	8.6	8.5	2.5
		N	**%**	**N**	**%**
Sex	*Female*	688,172	54.5	4,159	53.1
	Male	575,540	45.5	3,679	46.9
Marital status	*Single*	192,769	15.3	69	0.9
	Married	838,161	66.3	7,022	89.6
	Divorced	88,645	7.0	594	7.6
	Widowed	144,137	11.4	153	2.0
Education level	*≤primary*	314,675	24.9	876	11.2
	Junior sch.	327,780	25.9	2,615	33.4
	High sch.	416,101	32.9	3,086	39.4
	University	205,156	16.2	1,261	16.1
Occupation status	*Employed*	578,751	45.8	5,390	68.8
	Unemployed	62,859	5.0	440	5.6
	Homemaker	265,546	21.0	1,567	20.0
	Retired	296,398	23.5	125	1.6
Neigh. socio-econ. (quintiles)	*1 (less deprived)*	250,021	19.8	1,505	19.2
	2	257,525	20.4	1,409	18.0
	3	253,597	20.1	1,430	18.2
	4	257,566	20.4	1,534	19.6
	5 (more deprived)	245,003	19.4	1,960	25.0
Neigh. income (deciles)	*1 (lowest)*	8,812	0.7	30	0.4
	2	134,039	10.6	1,401	17.9
	3	125,689	9.9	513	6.5
	4	156,237	12.4	865	11.0
	5	134,277	10.6	647	8.3
	6	193,574	15.3	1,163	14.8
	7	179,106	14.2	1,116	14.2
	8	199,811	15.8	1,252	16.0
	9	63,980	5.1	381	4.9
	10 (highest)	68,187	5.4	470	6.0

* SIDRIA cohort: ~7000 Rome young parents; PREDICTOR panel: ~1000 subjects 65+ years old, representative of the population

Table S6. Exposure and covariate distributions in the main cohort and survey used for indirect adjustment of smoking and BMI in Switzerland

Covariate		**Cohort (N=4,188,175)**		**Survey* (N = 10,896)**	
		mean	**sd**	**mean**	**sd**
NO_2	*μg/m³*	23.7	7.4	23.6	7.7
$PM_{2.5}$	*μg/m³*	15.9	2.4	15.8	2.6
BC	*$10^{-5}m^{-1}$*	1.7	0.4	1.7	0.4
O_3	*μg/m³*	94.8	5.9	95.2	6.3
Age (baseline)	*yr*	52.7	15.2	53.4	15.1
Socio-econ. (neigh. 2001)	*score*	63.1	7.3	62.7	7.3
Unemploy. rate (neigh. 2001)	*%*	3.5	1.5	3.5	1.5
Education level (neigh. 2001)	*% low*	28.4	7.3	28.8	7.5
Education level (neigh. 2001)	*% high*	19.9	7.5	19.9	7.6
Socio-econ. (region 2001)	*score*	62.9	4.2	62.3	4.4
Unemploy. rate (region 2001)	*%*	3.5	0.8	3.5	0.9
Education level (region 2001)	*% low*	28.5	3.7	29.2	3.8
Education level (region 2001)	*% high*	19.8	4.1	19.6	4.3
		N	**%**	**N**	**%**
Sex	*Female*	2,179,587	52.0	6,121	56.2
	Male	2,008,588	48.0	4,775	43.8
Marital status	*Single*	585,510	14.0	1,745	16.0
	Married	2,900,333	69.3	6,983	64.1
	Divorced	362,642	8.7	1,115	10.2
	Widowed	339,690	8.1	1,053	9.7
Education level	*Low*	1,027,268	24.5	2,082	19.1
	Medium	2,208,181	52.7	6,226	57.1
	High	952,726	22.7	2,588	23.8
Occupation status	*Employed*	2,573,280	61.4	6,693	61.4
	Unemployed	90,238	2.2	166	1.5
	Homemaker	612,344	14.6	1,472	13.5
	Retired	912,313	21.8	2,565	23.5
Country of origin	*Local*	3,480,232	83.1	9,791	89.9
	Other	707,943	16.9	1,105	10.1
Mother tongue	*% German*	2,725,399	65.1	7,214	66.2
	% French	819,858	19.6	2,493	22.9
	% Italian	309,192	7.4	813	7.5
	% other	333,726	8.0	376	3.5

* Swiss Health Survey of 1992 (n~15,000)

2. Extended methods

2.1 Exposure models

Details of the ELAPSE exposure assessment models are reported in de Hoogh et al.[3] Briefly, we developed Europe wide models for annual average $PM_{2.5}$, NO_2, BC and warm and cold season O_3. The monitoring data, GIS data and modelling methods for ELAPSE closely followed our previous European modelling paper.[4] In this paper, models were developed based upon ESCAPE and AirBase routine monitoring data of the year 2010. An important finding was that models based on one monitoring database performed well when validated with the other database. We used models based on AirBase monitoring as the main exposure variable, because this modelling approach can be performed for multiple years. We selected 2010 as the primary year of modelling because 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 consistency, we used 2010 for NO_2 and O_3 as well for our main models.

Annual average concentration data for $PM_{2.5}$, NO_2 and O_3 (warm season average) for 2010 were derived from Airbase routine air pollution monitoring data for 543 sites ($PM_{2.5}$), 2399 sites (NO_2) and 1730 sites (O_3) spread across Europe. Models for BC were developed based upon ESCAPE monitoring data for 2010 (436 sites). As predictor variables we used road and land use data supplemented with satellite data and dispersion model estimates. The satellite data were the SAT $PM_{2.5}$ product (V3.01) at a 0.1° x 0.1° (~10 km) and two newly available products from the global dataset reported in van Donkelaar et al.[5] The pre-Geographically Weighted Regression dataset used here includes Aerosol Optical Density (AOD) from multiple satellite products (MISR, MODIS Dark Target, MODIS and SeaWiFS Deep Blue, and MODIS MAIAC) together with simulation-based sources, with information content below ~10km provided by the MAIAC AOD retrieval. NO_2 SAT estimates for 2010 were derived from the tropospheric NO_2 columns measured with the OMI (Ozone Monitoring Instrument) on board the Aura satellite. Like $PM_{2.5}$, the satellite column-integrated retrievals were related to ground-level concentrations using the global GEOS-Chem model, producing an annual gridded NO_2 surface at a 10km resolution. Pollutant estimates for 2010 from two long range CTM's were obtained as potential predictor variables in the models. Annual $PM_{2.5}$, NO_2 and O_3 estimates were derived from the MACC-II ENSEMBLE model at a 0.1º x 0.1º (~10km) resolution. We additionally used a dataset from the Danish Eulerian Hemispheric Model (DEHM) for $PM_{2.5}$, NO_2, O_3 and BC at a monthly (temporal) 26 x 26km (spatial) resolution (downscaled from an original 50 x 50km resolution using bi-linear interpolation).[6] Annual DEHM averages were calculated for NO_2, $PM_{2.5}$, BC and O_3. Road data, classified as 'all' and 'major' roads, was extracted from the 1:10,000 EuroStreets digital road network. Traffic intensity data were not used as the data was not available consistently across Europe. Land cover data were extracted from European Corine Land Cover 2006 data. Elevation was extracted from the SRTM Digital Elevation Database version 4.1 which has a resolution of approximately 90 m. Population data (1 km resolution) for 2011 was obtained from Eurostat.

Land use regression models were developed using the supervised linear regression approach used within ESCAPE. 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%, 60% and 51% of the variability in measured concentrations in 5-fold cross-validation for $PM_{2.5}$, NO_2, O_3 and BC respectively. Performance of the models in specific study areas or at lower concentrations differed but was generally lower than the overall performance (Table S7).[3] The performance of the model measured by the R^2 but not the RMSE was lower for $PM_{2.5}$ and BC when restricted to lower levels. Lower variability in subsets of low concentrations has likely contributed to the decrease in R^2. Below 10 $\mu g/m^3$ of $PM_{2.5}$ few sites remained to evaluate the model performance. For NO_2 the model performance was only modestly worse at low levels. For ozone, the model performed poorly when restricted to concentrations below 80 $\mu g/m^3$ (Table S7).

Table S7. Validation of the ELAPSE exposure model at low pollution levels. HOV refers to the five-fold hold-out validation approach

	Validation at ELAPSE sites (HOV)				**Validation at ESCAPE sites**		
$PM_{2.5}$							
	R^2	RMSE	n		R^2	RMSE	n
All	0.664	2.97	543		0.648	3.41	416
<25 µg/m^3	0.649	2.70	523		0.601	2.95	390
<20 µg/m^3	0.630	2.34	439		0.612	2.37	327
<15 µg/m^3	0.532	1.92	230		0.593	1.58	191
<12 µg/m^3	0.379	1.55	130		0.405	1.32	118
<10 µg/m^3	0.379	1.26	86		0.271	1.05	74
NO_2							
	R^2	RMSE	n		R^2	RMSE	n
All	0.575	9.51	2399		0.494	11.47	1396
<40 µg/m^3	0.613	5.88	2008		0.507	6.14	1116
<30 µg/m^3	0.620	4.48	1520		0.491	4.74	844
<20 µg/m^3	0.572	3.20	841		0.384	3.31	433
BC							
	R^2	RMSE	n		R^2	RMSE	n
All	NA	NA	NA		0.514	0.58	433
<3*10-5/m					0.424	0.45	390
<2.5*10-5/m					0.375	0.39	351
<2*10-5/m					0.311	0.33	277
<1.5*10-5/m					0.343	0.21	162
<1*10-5/m					0.119	0.14	59
<0.5*10-5/m					0.717	0.07	3
O_3 warm season							
	R^2	RMSE	n		R^2	RMSE	n
All	0.599	8.63	1728		NA	NA	NA
< 120 µg/m^3	0.595	8.49	1716				
< 100 µg/m^3	0.448	7.77	1366				
< 80 µg/m^3	0.073	7.78	393				
< 60 µg/m^3	0.068	6.32	40				

2.2 Back- and forward-extrapolation of exposures

Our main model based on 2010 monitoring represents exposure towards the end of follow-up for most of the administrative cohorts. We estimated pollutant concentrations for each year from recruitment to end of follow-up for $PM_{2.5}$, NO_2, BC and O_3 using back- and forward-extrapolation methods. This was achieved by using estimated concentrations from the Danish Eulerian Hemispheric Model (DEHM).[6] DEHM models monthly average concentrations across Europe at 26 x 26 km spatial resolution back to at least 1990. The rationale to perform back- and forward-extrapolation by modelled concentrations is 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 $PM_{2.5}$. We used monitoring data to compare temporal patterns of modelled and measured concentrations for countries with measurements. For application to the cohorts, we calculated population weighted average concentrations at the NUTS-1 spatial scale (Nomenclature of territorial units for statistics), allowing different spatial trends within Europe. The NUTS classification is a hierarchical system for dividing up the economic territory of the EU and the UK for the purpose of the collection, development and harmonization of European regional statistics. NUTS-1 reflect major socio-economic regions. NUTS-1 may be an entire (small) country or parts of a country (e.g., four regions in the Netherlands and 14 regions in France). We extrapolated concentrations, using both a difference and a ratio method with

2010 as the baseline. With the difference method the concentration difference between a year and 2010 from the DEHM model is added to all cohort exposures for that year in the same NUTS-1 area. With the ratio method the concentration ratio between a year and 2010 from the DEHM model is used to multiply all cohort exposure for that year in the same NUTS-1 area.

2.3 Road traffic noise

Estimates of traffic noise exposure at the residential addresses of the cohorts' participants were available for five of the seven administrative cohorts.

In Belgium, noise is available for the Brussels Capital Region. In particular, noise levels are measured through 17 permanent measurement stations situated in strategical places of the BCR, these stations can measure the influence of a single means of transportation and thereby register aerial, railway and road noise. Additionally, mobile sound level meters were used to validate the model results. Average noise levels are calculated for the year 2016 and for 4 indicators: L_{day} (07h-19h), $L_{evening}$ (19h-23h), L_{night} (23h-7h) and L_{den} (energetic combination of L_{day}, $L_{evening}$, L_{night}= 24h). For the calculation of the L_{den} global indicator, $L_{evening}$ and L_{night} indicators are rescaled by a 5 db(A) increase for $L_{evening}$ and by a 10 dB(A) increase for L_{night} for the greater nuisance experienced when exposed to noise during those hours.
For the purposes of the ELAPSE project, Lden was collected. Noise maps were delivered in GeoTiff files at fine spatial scale of 10x10-m. Data were made available for the year 2016 and delivered by Brussels Environment, the official regional environment agency.

In the Netherlands, we estimated annual average traffic noise exposure by the Standard Model Instrumentation for Noise Assessments (STAMINA), which has been developed by the Dutch National Institute for Public Health and the Environment. The STAMINA model implements the standard Dutch Calculation method for traffic and industrial noise and uses detailed information on the types of noise source and ground data. The model has a resolution of 10x10 m around the noise sources. At increasing distances from the noise source, the resolution gradually increases to at most 80x80 m (reference). Daily average (Lden) and nighttime average (Lnight) road traffic and railway noise exposure were estimated for 2011.

In Norway, noise exposure from transport was obtained from the Norwegian national noise model, conducted by Statistics Norway in 2014. The model utilizes existing noise mapping performed by sectoral authorities and research environments but perform additional calculations where noise assessments have not previously been conducted. The calculations are performed using Geographic Information Systems (GIS) and assess annual average 24-hour noise level (LAeq, 24h) at each residential address point for all dwellings in Norway. Input data to the 3D terrain model including all buildings (polygons) includes source specific emission data, traffic frequency, speed, ground properties and noise screens. For calculation of road traffic noise, the tool NorStøy was used. Norstøy is developed by SINTEF and is based on the prediction model Nord2000,[7] a state-of-the-art model for outdoor sound propagation, resulted from work at SINTEF in cooperation with the other Nordic technology research institutes. A model for traffic on smaller roads was employed by the national noise model to include noise from smaller roads in the calculations.[8] Aircraft noise was calculated by the Norwegian prediction model for aircraft noise, NORTIM.[9] All large airports and most of the smaller airports are included in the national noise model. The Nordic prediction method for railway noise, Nord96, was used to calculate noise from railway, trams and subway.[10] In the Norwegian analyses we adjusted for the annual average 24h noise level (LAeq,24h) from road traffic, which is the major source. To capture the exposure from additional transport noise sources, we included a dichotomous variable of 1 if LAeq,24h was above 55 dB from either aircraft or railway/trams/subway, and 0 otherwise.

In Rome, road traffic noise exposure was estimated, for all the addresses of the participants for the year 2009, using the calculation software Sound-Plan 7.4 as indicated by the Good Practice Guides of the European Community. The model took into consideration the following parameters: a) number of vehicles (equivalent cars) per hour; b) average speed during rush hour; c) traffic model parameters (capacity, alpha / beta). Road traffic was estimated, at the level of the facade of the most exposed residence address, for the day, evening and night, and was also expressed as L_{den} (indicator that takes into account daytime, evening and night noise) by applying a reduction of 5-dB penalty for the evening and 10-dB for the night). In the ELAPSE analyses, we adjusted for road traffic noise using the L_{den} variable as a continuous covariate. Noise data is available for the entire Rome Longitudinal Study.

In Switzerland, road traffic noise emissions are calculated using sonROAD[11] and propagation computed via the propagation model of StL-86.[12] Railway noise emissions are calculated using sonRAIL[13] and propagation computed using the Swiss railway noise model SEMIBEL.[14]
Aircraft noise is calculated via FLULA2,[15] based on radar data for Zurich. For Geneva and Basel, exposure is calculated based on traffic statistics from the Federal Office of Civil Aviation along with available acoustic footprints from the years 2000 and 1999, respectively. For Payerne (military airport), noise exposure estimates were computed based on idealized

flight paths, number of flights and approximate operation times. For each building in Switzerland, noise exposure is estimated at pre-defined façade points. A maximum of three façade points, spaced by at least 5 m, were assigned to each building façade by floor. We calculate the L_{den} (defined as the weighted energetic average of $L_{eq,day}$ (07:00–19:00), $L_{eq,evening}$ (19:00–23:00) and $L_{eq,night}$ (23:00–07:00) with a respective penalty of 5 and 10 dB applied to the evening and night) for each noise source. The energetic sum of the three source-specific L_{den} values is also computed to derive total transportation noise, at every façade point. For the purpose of the ELAPSE project, noise exposure from 2001 has been used to match SNC baseline. The above-mentioned "total" variable is the one used in ELAPSE models.

2.4 Model specification

All analyses were performed per individual cohort because privacy regulations prevented data transfer to a central database. We specified three models with increasing levels of adjustment for confounding.

Model 1 included only age (time axis), sex (strata), and calendar time (year of enrolment).

Model 2 included all individual level variables available within each cohort. Availability of these covariates differed by administrative cohort. For example, the English administrative cohort had information on individual lifestyle covariates from primary care records (smoking, BMI), but no information on individual socio-economic status. The other administrative cohorts had individual data on demographic variables like education (Swiss, Rome, Norwegian), household income (Dutch, Danish, Norwegian) or employment status (Rome, Danish, Norwegian) that characterize socioeconomic status.

The main model is Model 3, where area-level socio-economic status (SES) variables at the regional and neighbourhood spatial scale were added. Regions were important for national cohorts (all except Rome), and were defined differently in each country, based on country-specific administrative units. Neighbourhoods were defined as smaller units, representing parts of a city, with about 1,000-10,000 people, with some differences across cohorts. SES has multiple dimensions, including income, education, occupation and employment. We used national composite scores that combine the different dimensions and in addition the main individual components as the association with air pollution and health may differ between dimensions. SES scores at regional scale were calculated by aggregating the raw variables to region level and then calculated the SES score. Similarly, SES scores at neighbourhood level were defined by aggregating the raw variables from the smaller spatial units available.

Table S8 reports the individual and area-level variables available in each cohort and used in the model (model 3).

Table S8. Individual-level and area-level variables available in each cohort and adjusted for in the model

	Belgian cohort	**Danish cohort**	**Dutch cohort**	**English cohort**	**Norwegian cohort**	**Rome cohort**	**Swiss cohort**
Individual-level covariates							
Age	time axis	time axis	time axis	time axis	time axis	time axis	time axis
Sex	strata	strata	strata	strata	strata	strata	strata
Smoking status	-	-	-	categorical	-	-	-
BMI	-	-	-	quadratic	-	-	-
Country origin	categorical	categorical	categorical	-	-	-	categorical
Household income	-	deciles	deciles	-	quartiles	-	-
Marital status	categorical	-	categorical	-	categorical	categorical	categorical
Education level	categorical	-	-	-	categorical	categorical	categorical
Occupational status	categorical	categorical	-	-	categorical	categorical	categorical
Mother tongue	-	-	-	-	-	-	categorical
Area-level covariates (at neighborhood and regional level)							
Income	Linear	Linear	Linear	-	Linear	Deciles	-
Education	Linear	Linear	-	-	Linear	Linear	Linear
Unemployment rate	Linear	Linear	Linear	-	Linear	Linear	Linear
Non-western ethnic	Linear	-	Linear	-	-*	-	-
SES score	-	-	Linear	Deciles	-	Quintiles	Linear

* Variable available but not used in the analyses due to high correlations with other neighbourhood variables

In all models we further adjusted the standard errors of the effect estimates for clustering inherent in the data due to the subjects' residence in the same neighbourhood. The variance correction applies a robust or sandwich-type variance estimator to account for the clustering of subjects.[16,17]
To address the lack of information of lifestyle factors, we explored two approaches: (1) indirect adjustment using available survey data, and (2) using information on area-level (neighbourhood and region) morbidity or mortality from lung cancer, COPD and diabetes. See section 2.6 for further details.

2.5 Concentration-response relationships

2.5.1 Cohort-specific analysis

In each cohort, we adopted a three-way strategy to investigate the shape of the concentration-response functions between the four pollutants and the study outcomes, with special attention to the lowest ranges of air pollutants distributions.

First, we used natural splines with 3 degrees of freedom (d.f.), following earlier analysis in the CanCHEC cohort,[18,19] as a flexible method allowing multiple shapes in different parts of the exposure distribution. Natural splines are cubic polynomial-like functions in intervals of the variable distribution as these are defined by the knots (used in formulating basis functions) and impose a smoothness criterion to satisfy certain differentiability properties. The degrees of freedom of a natural spline correspond to the number of knots plus 1 (as implemented in the context of our models). The choice of this number is critical as increasing the number of knots may overfit the data and increase the variance, whilst decreasing the number of knots may result in a rigid and restrictive function that has more bias.[20,21] We opted for 3 d.f. (corresponding to two inner knots equally spaced and located at terciles of exposure distribution) as a good compromise between model parsimony and ability to capture non linearities in different parts of the curve. The R library "splines" and the function ns were used to fit the splines.

Second, we applied the SCHIF function used in the Canadian MAPLE study.[22,23] We used version 2.10 (February 24, 2016) of the SCHIF code provided by Prof. Burnett, adapted to the Cox model 3 applied in our analysis. In contrast to the splines, the SCHIF methodology specifies a range of functions with a plausible shape, including sublinear, linear and supra-linear functions.[23] A detailed description of the SCHIF method has been included in the MAPLE study report.[24]

Third, we specified linear models in subsets of the concentration range, defined by removing concentrations above a certain value from the analysis, such as for $PM_{2.5}$ below 25 (EU limit value), 20, 15, 12 (US EPA National Ambient Air Quality Standard) and 10 µg/m3 (WHO Air Quality Guideline value). The purpose of this analysis is to directly answer the question: "does air pollution affect mortality at low exposure levels"? We specifically evaluated the associations:

- $PM_{2.5}$: below 25, 20, 15, 12 or 10 $\mu g/m^3$
- NO_2: below 40, 30 or 20 $\mu g/m^3$
- BC: 3.0, 2.5, 2.0, 1.5 or $1.0*10^{-5}m^{-1}$

2.5.2 Meta-smoothing

We obtained meta-analytical curves of the concentration-response functions between the four pollutants and non-accidental mortality by applying the "meta-smoothing" approach on the output of the natural spline analyses. First, for each cohort and pollutant we obtained predictions (and standard errors) of the log-hazard ratios of natural mortality per each 0.1 mg/m^3 increment in the pollutant-specific concentrations (0.01 for BC). As these were all centred on the mean of the cohort-specific distributions, as a second step we rescaled the predictions so to represent log-hazard ratios of mortality compared with common values across cohort, equal to 13.5 mg/m^3 for $PM_{2.5}$, 35 mg/m^3 for NO_2, $1.9*10^{-5}$/m for BC, and 80 mg/m^3 for warm season O_3. Such values were chosen in order to be included in the concentration distributions of all cohorts. Third, we ran univariate random-effects meta-analyses on each 0.1-unit increment (0.01 for BC) and plotted the resulting curves.

2.6 Indirect adjustment for smoking and BMI

We applied the indirect adjustment method proposed by Shin et al. (2014).[25] The method involves the use of ancillary information from surveys that are highly representative of the subjects in the cohort, to adjust the estimated hazard ratios for missing confounders such as smoking and BMI. The method uses the relationship between air pollution exposure and lifestyle in an external (survey) population and applies that relationship to the cohort missing lifestyle information. The Shin method further needs a risk function for the missing confounder variable. We applied the Shin method for non-accidental mortality and the key potential confounders smoking status and BMI. We focused on smoking and BMI, because these were considered critical confounders in the WHO systematic review of outdoor air pollution.[26] We applied the method in four steps. First, we assessed the comparability of the survey and cohort. Second, we assessed the quantitative relationship between air pollution and smoking status and BMI in the survey. Third, we obtained the HR of smoking and BMI by external analysis in the pooled cohort of the ELAPSE study. Fourth, we used the above information in the adjustment formulas proposed by Shin.

As Shin and co-workers emphasize the need for "assessing the adequacy of the ancillary health studies in representing the cohort study", in the first step we compared the distributions of air pollution, age, sex and other variables available in the administrative cohorts between the administrative cohorts and the available surveys (Tables S1-S6). Concerns should be raised about using the ancillary data if these distributions are not similar. The second step was to assess whether BMI and smoking were associated with the air pollution estimates using a multiple linear regression model controlling for the other covariates in the Model 3. This step was on whether these variables could act as potential confounders in the final epidemiological models. The quantitative results were applied in the adjustment procedure.

Subsequently we adjusted the estimates from the main Cox model (model 3) by using the estimates of the association between the missing risk factors (BMI and smoking) and the health outcome. Shin et al., 2014 proposed to obtain these from the literature.[25] In ELAPSE we estimated the association between BMI and total mortality from the pooled cohorts' data. The indirect adjustment method incorporates in the formula the association between observed covariates (all variables in the model including air pollution) in the administrative cohort with the missing covariates (BMI and smoking) that are acquired from the ancillary study data. Specifically, the indirectly adjusted parameter is given by $\tilde{\beta} = \hat{\gamma} - \bar{\Delta}\tilde{\lambda}$ where $\hat{\gamma}$ is the vector of the unadjusted estimates for the air pollution effects, $\bar{\Delta}$ is a matrix of estimates for the associations between the confounders from the ancillary dataset and the observed variables, $\tilde{\lambda}$ is a vector of the regression parameter estimates of the BMI and smoking risk factors on the health outcome obtained from external data. The variance of the adjusted estimates also incorporates the variance of the estimates of the observed variables, the variance-covariance matrix of the estimates of the missing factors obtained from the external data and the variance-covariance matrix of the estimates for the associations between observed variables and missing factors based on ancillary survey data.

As a complementary approach to the indirect adjustment method described above, we collected data on area-level prevalences of COPD, lung cancer and diabetes, and adjusted for them as proxies for smoking and BMI. Specifically, for each cohort we used age-standardized area-level prevalences of diseases related to smoking and obesity: lung cancer, COPD and diabetes. These variables were added to model 3 as linear terms as an alternative approach to adjust for confounding from smoking (COPD and/or lung cancer prevalences) and BMI (diabetes prevalence). Details on cohort-specific sources for area-level data on COPD, lung cancer and diabetes are reported below:

- Belgian cohort: Area-level standardised rates based on mortality data (same source as the ELAPSE study). ICD-10 code: #1 COPD (w/o asthma) - J40-J44, J47 — #2 Diabetes - E10-E14 —#3 Lung cancer - C34.0-C34.9.
- Danish cohort: The population and causes of death registers from 2000 were obtained for calculating age-standardized municipality-level mortality rates from lung cancer, COPD, and diabetes.
- Dutch cohort: For lung cancer, regional age-standardized smoking attributable mortality fractions were based on observed lung cancers rates during 2004-2008; for diabetes, prescribed medications for diabetes (ATC4-code: A10B) were collected, based on national data on prescriptions.
- Norwegian cohort: The source used is the Norwegian Municipal Health Statistics Bank. From this source, lung cancer data: Norwegian Cancer Registry; diabetes data: Norwegian Prescription Registry.
- Rome cohort: Lazio Region hospital discharge records were used to compute age-standardized rates of lung cancer, diabetes and COPD.

2.7 Sensitivity analyses

We conducted a number of sensitivity analyses to evaluate the robustness of the main findings to modelling choices or co-exposures. Specifically:

- we fitted two-pollutant models for all combinations of the four main pollutants, by adding them as linear terms in the main model;
- we replaced 2010 exposures with those extrapolated at baseline year for each cohort, and added them as linear terms to the main model, using both the difference and the ratio methods previously described;
- we ran time-varying analysis to account for temporal changes in air pollution during follow-up. Specifically, for each cohort we split individual follow-up times by year and assigned each subject the annual average air pollution back- and forward-extrapolated to each year as the relevant exposure term, accounting for residential history during follow-up. Because of concerns with bias due to time trends in air pollution and mortality in the time-varying analysis, we additionally specified strata for calendar years of follow up. Once the adjustment model was defined, we inserted the air pollutant as either a linear term, or a natural spline with 3 d.f., to explore the shape of the concentration-response function between time-varying exposures and non-accidental mortality;
- we adjusted for traffic noise exposure (in the five cohorts with such data) by adding L_{den} as a linear term in the cardiovascular mortality-air pollution models.

3. Extended results

3.1 The study area

A map of the study areas is displayed in Figure S1.

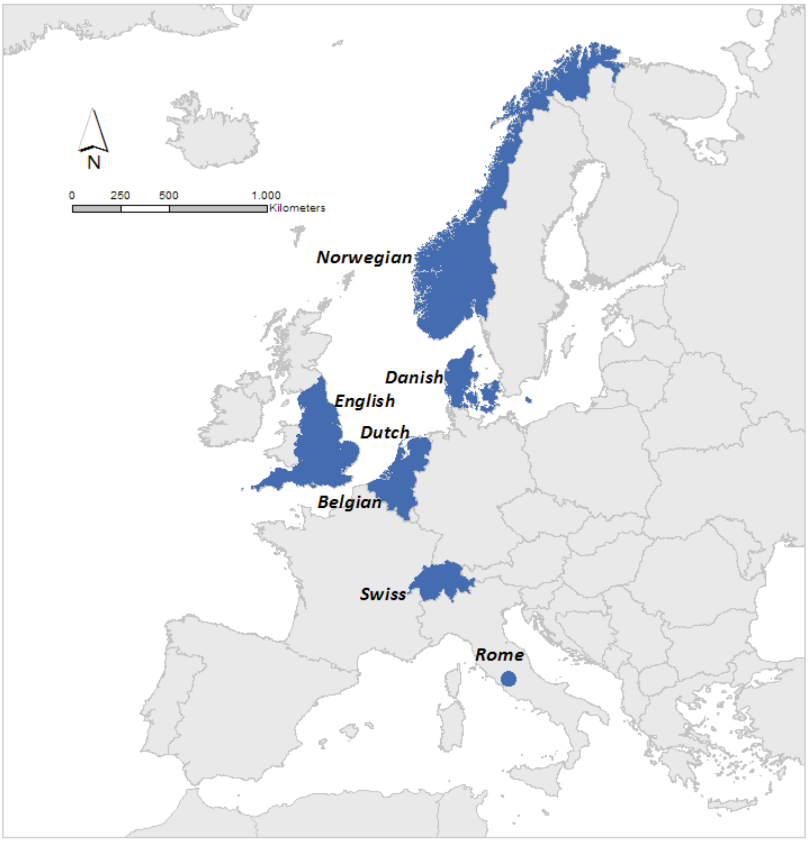


Figure S1. Map of Europe and location of the seven administrative cohorts

3.2 Correlations among air pollutant concentrations

Table S9 displays cohort-specific correlation matrices of the 4 air pollutants estimated at the addresses of the cohorts participants.

Table S9. Pearson correlation coefficients between pairs of air pollutants concentrations estimated at the addresses of the cohorts participants

Cohort	$PM_{2.5}$ - NO_2	$PM_{2.5}$ - BC	$PM_{2.5}$ - O_3	NO_2 - BC	NO_2 - O_3	BC - O_3
Belgian	0.64	0.61	-0.63	0.86	-0.80	-0.72
Danish	0.60	0.70	-0.50	0.89	-0.65	-0.67
Dutch	0.51	0.50	-0.41	0.88	-0.77	-0.64
English	0.67	0.67	-0.31	0.84	-0.72	-0.50
Norwegian	0.86	0.84	-0.65	0.92	-0.81	-0.78
Rome	0.76	0.64	-0.68	0.91	-0.80	-0.82
Swiss	0.71	0.70	-0.60	0.93	-0.67	-0.68

3.3 Main associations between air pollutants and mortality

Table S10 reports the results of the different models 1-2-3 with increasing level of covariate adjustment. Model 1 was adjusted for age (time axis), sex (strata) and calendar time (year of enrolment). Model 2 was further adjusted for all the available individual-level covariates (as described in Table 1). Model 3 (our "main" model" was further adjusted for area-level socio-economic status variables at the regional and neighborhood spatial scale. All 3 models were run on the subset of observations with complete data on all covariates from model 3, in order to facilitate comparisons across models. We observed a general trend of increasing association estimates when passing from less adjusted models (model 1) to fully adjusted models (model 3).

Table S10. Association between air pollutants and cause-specific mortality in seven administrative cohorts, from models with increasing levels of adjustment for individual and area-level confounders: Hazard Ratios (HR), and 95% Confidence Intervals (95% CI) per fixed increments* of the pollutants, results from the random-effects meta-analysis

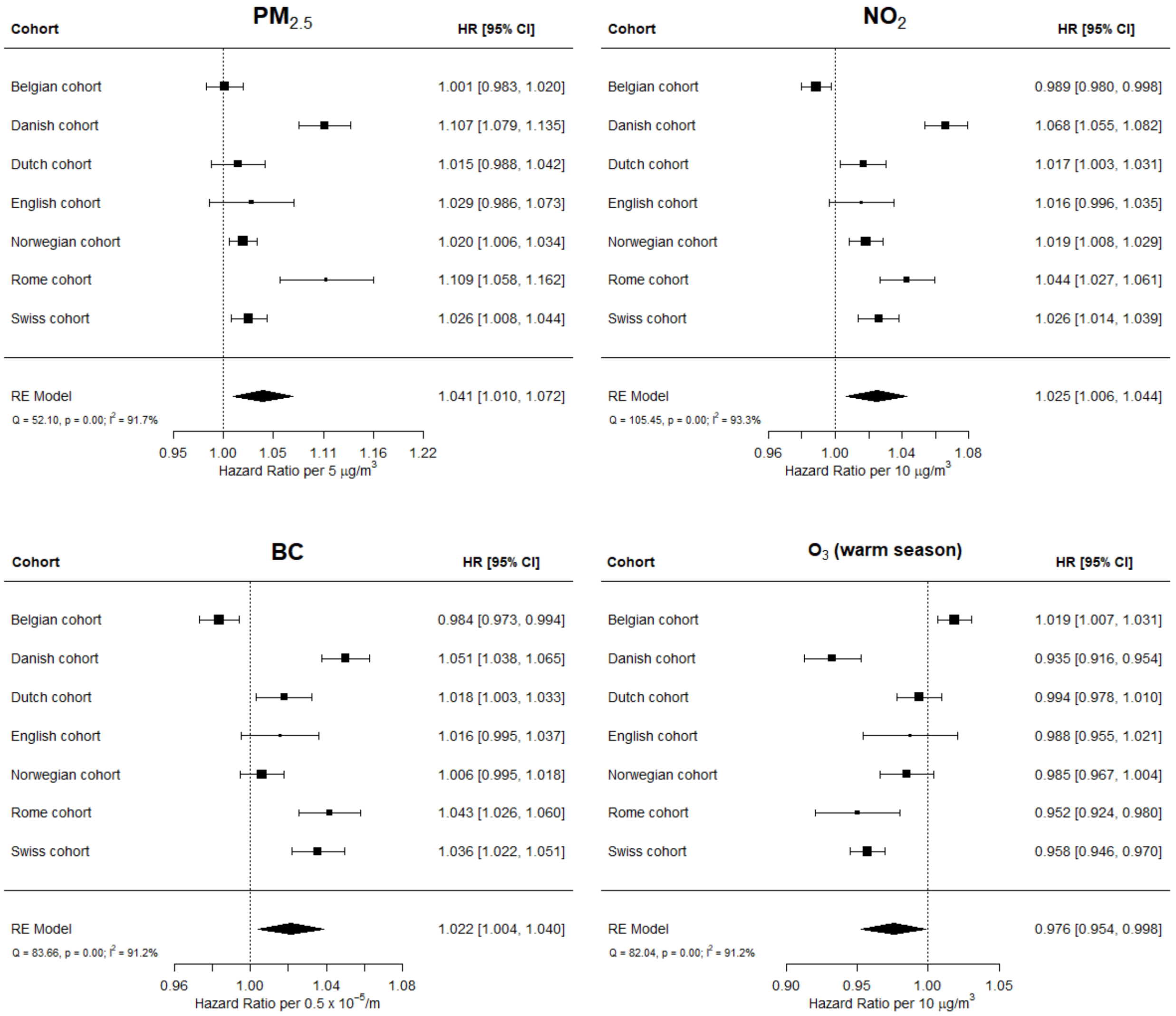
	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Main model HR (95% CI)
Non-accidental mortality			
$PM_{2.5}$	1.004 (0.967, 1.044)	1.021 (0.986, 1.058)	1.053 (1.021, 1.085)
NO_2	1.010 (0.991, 1.030)	1.017 (1.002, 1.031)	1.044 (1.019, 1.069)
BC	1.015 (0.996, 1.035)	1.028 (1.007, 1.048)	1.039 (1.018, 1.059)
O_3 (warm season)	0.967 (0.934, 1.002)	0.968 (0.937, 1.000)	0.953 (0.929, 0.979)
Cardiovascular mortality			
$PM_{2.5}$	1.010 (0.943, 1.081)	1.025 (0.976, 1.077)	1.041 (1.010, 1.072)
NO_2	0.999 (0.957, 1.042)	1.008 (0.982, 1.036)	1.025 (1.006, 1.044)
BC	1.004 (0.960, 1.051)	1.014 (0.984, 1.046)	1.022 (1.004, 1.040)
O3 (warm season)	0.984 (0.925, 1.048)	0.991 (0.962, 1.022)	0.976 (0.954, 0.998)
Respiratory mortality			
$PM_{2.5}$	1.068 (0.994, 1.147)	1.084 (1.014, 1.158)	1.064 (1.013, 1.118)
NO_2	1.042 (1.009, 1.076)	1.060 (1.021, 1.101)	1.058 (1.024, 1.093)
BC	1.053 (1.018, 1.088)	1.068 (1.032, 1.105)	1.053 (1.021, 1.085)
O3 (warm season)	0.947 (0.889, 1.009)	0.933 (0.870, 0.999)	0.948 (0.910, 0.988)
Lung cancer mortality			
$PM_{2.5}$	1.111 (1.015, 1.217)	1.137 (1.052, 1.229)	1.102 (1.036, 1.172)
NO_2	1.083 (1.044, 1.123)	1.103 (1.069, 1.138)	1.093 (1.053, 1.134)
BC	1.092 (1.049, 1.136)	1.108 (1.071, 1.146)	1.078 (1.038, 1.118)
O3 (warm season)	0.905 (0.852, 0.961)	0.893 (0.849, 0.939)	0.924 (0.887, 0.963)

Model 1 included only age (time axis), sex (strata), and calendar time (year of enrolment). Model 2 included all individual level variables available in each cohort. Main model added area-level socio-economic status (SES) variables at the regional and neighbourhood spatial scale

* Fixed increments were: 5 $\mu g/m^3$ for $PM_{2.5}$, 10 $\mu g/m^3$ for NO_2 and O_3, and 0.5*10-5/m for BC

Figures S2-S4 present cohort-specific and meta-analytical results of the associations between the four air pollutants and cardiovascular (Fig. S2), respiratory (Fig. S3) and lung cancer mortality (Fig. S4) in the seven administrative cohorts. We observe large differences between cohort-specific estimates, also reflected in the high values of the Q and I^2 statistics from the random-effects meta-analysis. Meta-analytical estimates show significant associations between all exposures and all outcomes, highest for lung cancer mortality.

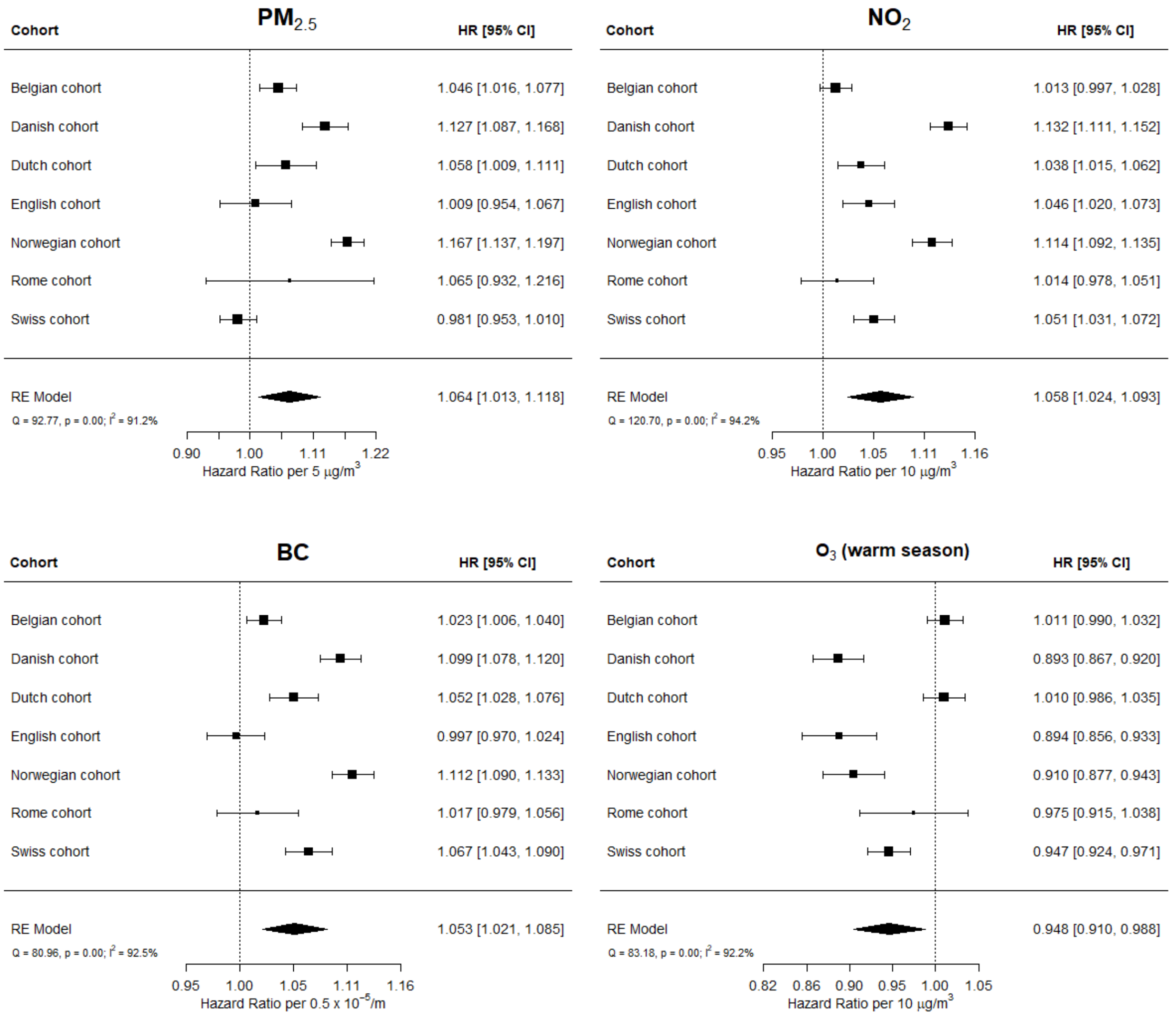
Figure S2. Forest plots of the association between air pollutants and cardiovascular mortality in the seven administrative cohorts: Hazard Ratios (HR), and 95% Confidence Intervals (95% CI) per fixed increments* of the pollutants. Cohort-specific and meta-analytical results.



The size of the squares is proportional to the weight of the estimate in the meta-analysis; Q is the Cochrane's statistic of heterogeneity of cohort-specific estimates, with p being its p-value; I^2 represents the proportion of total variation in effect estimates due to between-cohorts heterogeneity

* Fixed increments were: 5 µg/m^3 for $PM_{2.5}$, 10 µg/m^3 for NO_2 and O_3, and 0.5*10-5/m for BC

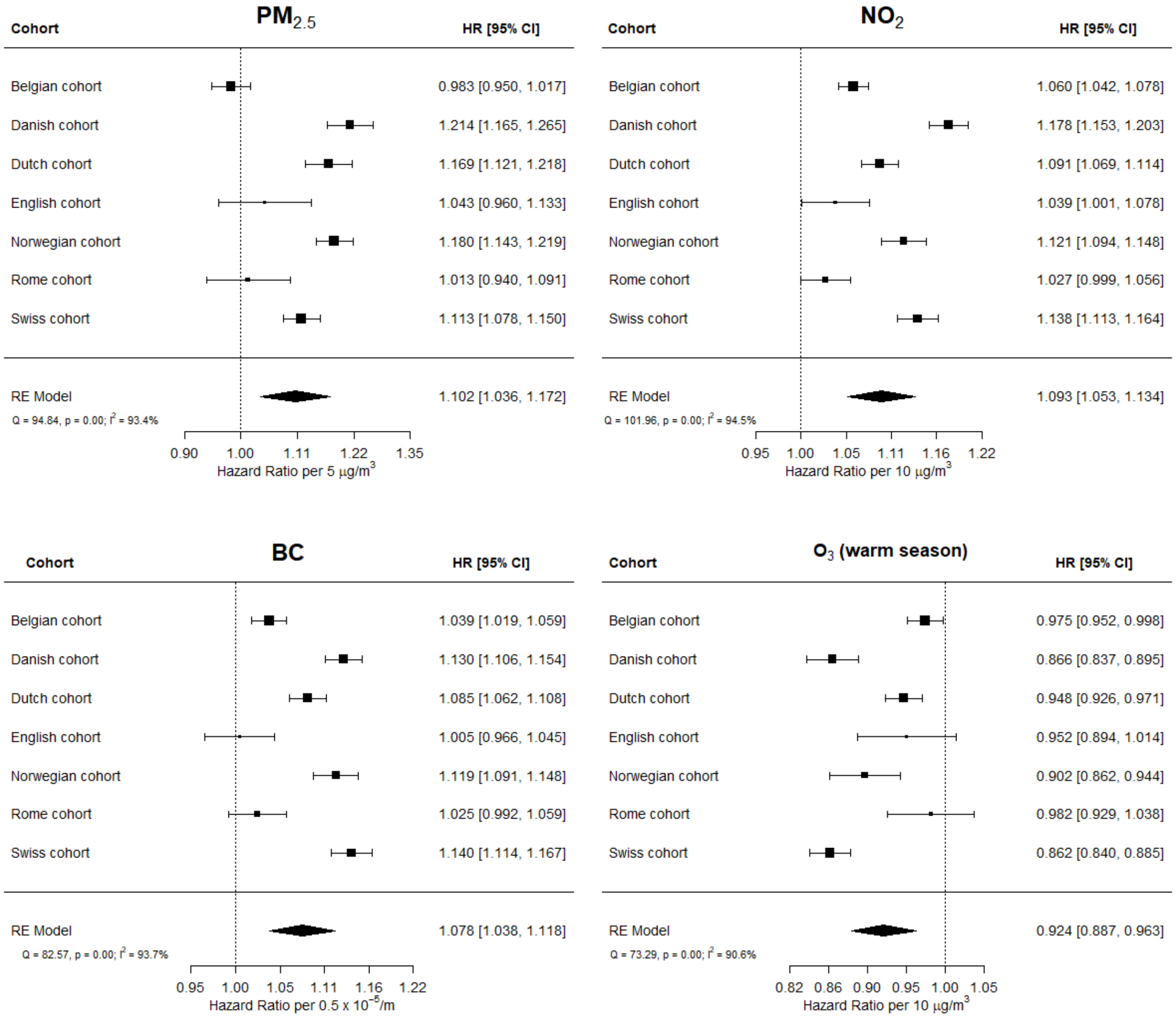
Figure S3. Forest plots of the association between air pollutants and respiratory mortality in the seven administrative cohorts: Hazard Ratios (HR), and 95% Confidence Intervals (95% CI) per fixed increments* of the pollutants. Cohort-specific and meta-analytical results



The size of the squares is proportional to the weight of the estimate in the meta-analysis; Q is the Cochrane's statistic of heterogeneity of cohort-specific estimates, with p being its p-value; I^2 represents the proportion of total variation in effect estimates due to between-cohorts heterogeneity

* Fixed increments were: 5 µg/m^3 for $PM_{2.5}$, 10 µg/m^3 for NO_2 and O_3, and 0.5*10-5/m for BC

Figure S4. Forest plots of the association between air pollutants and lung cancer mortality in the seven administrative cohorts: Hazard Ratios (HR), and 95% Confidence Intervals (95% CI) per fixed increments* of the pollutants. Cohort-specific and meta-analytical results



The size of the squares is proportional to the weight of the estimate in the meta-analysis; Q is the Cochrane's statistic of heterogeneity of cohort-specific estimates, with p being its p-value; I^2 represents the proportion of total variation in effect estimates due to between-cohorts heterogeneity

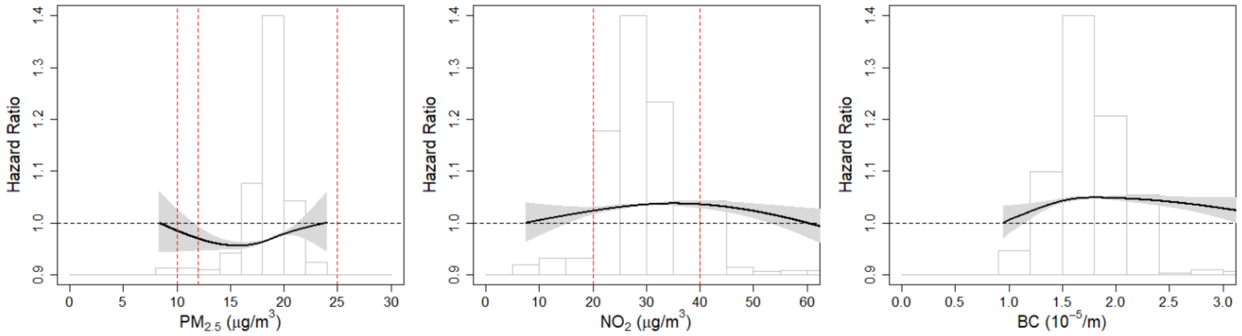
* Fixed increments were: 5 µg/m^3 for $PM_{2.5}$, 10 µg/m^3 for NO_2 and O_3, and 0.5*10-5/m for BC

3.4 Concentration-response relationships

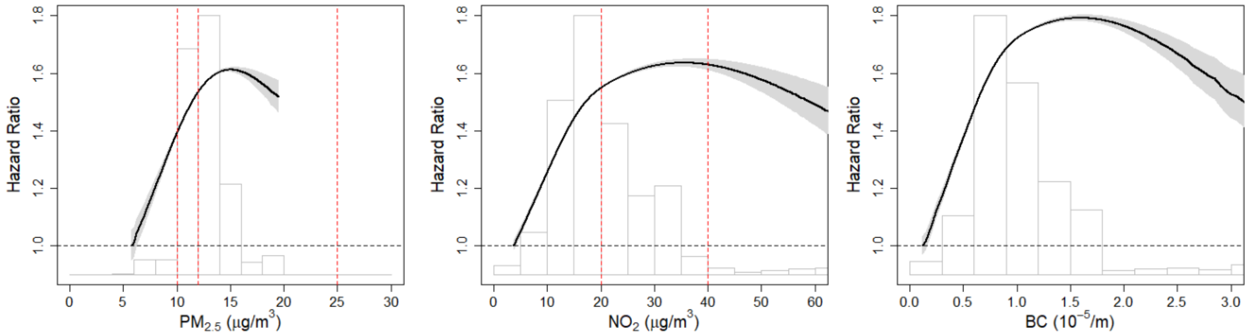
Figures S5 and S6 present the cohort-specific results of the concentration-response functions between the four air pollutants and non-accidental mortality, using natural splines (Figure S5) and the SCHIF methodology (Figure S6), respectively. We observe some degree of heterogeneity among cohorts, especially for $PM_{2.5}$, but most of the curves are consistent with increasing hazard ratios per increasing levels of air pollution, especially at the lower ends of air pollutants' distributions.

Figure S5. Concentration-response functions of the association between air pollutants and non-accidental mortality in the seven administrative cohorts: air pollutants modelled with natural splines with 3 degrees of freedom (grey regions identify 95% confidence bands)

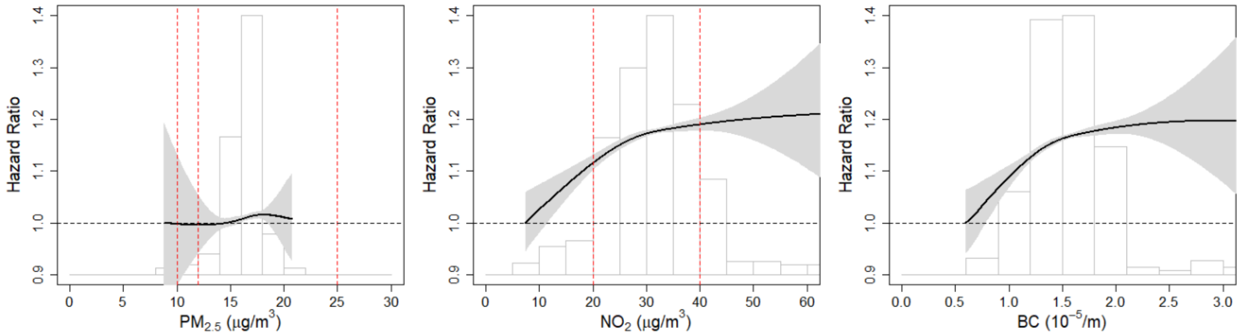
Belgian cohort



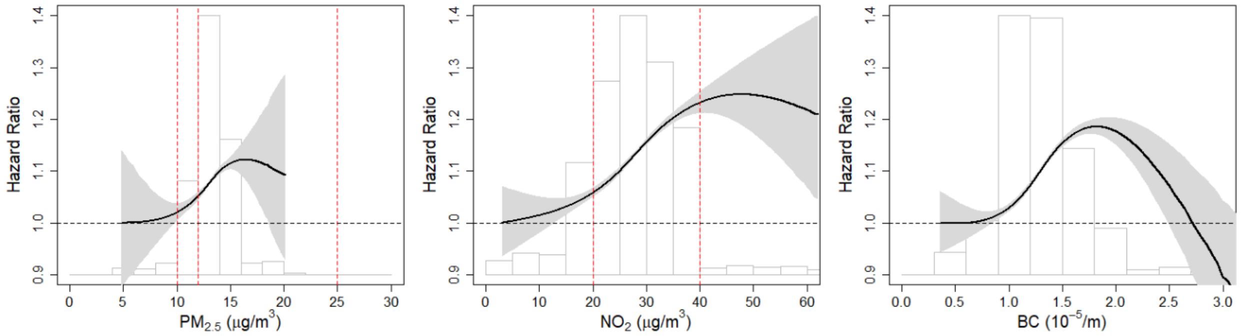
Danish cohort



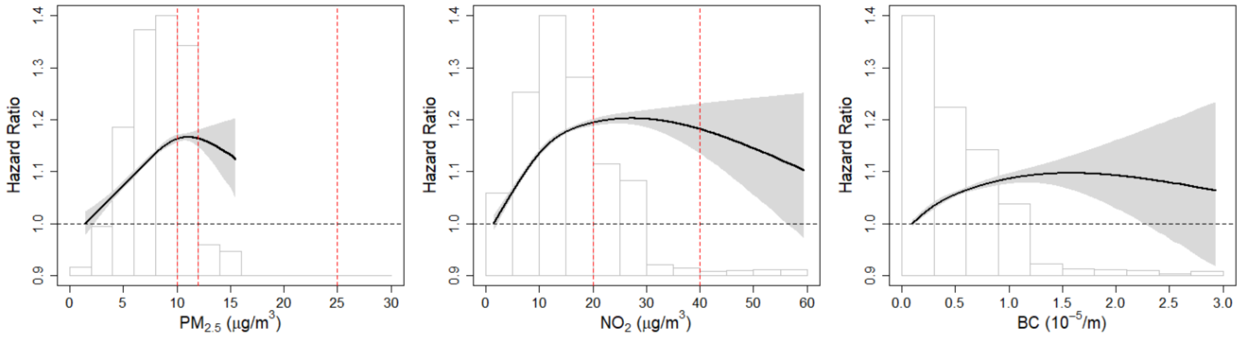
Dutch cohort



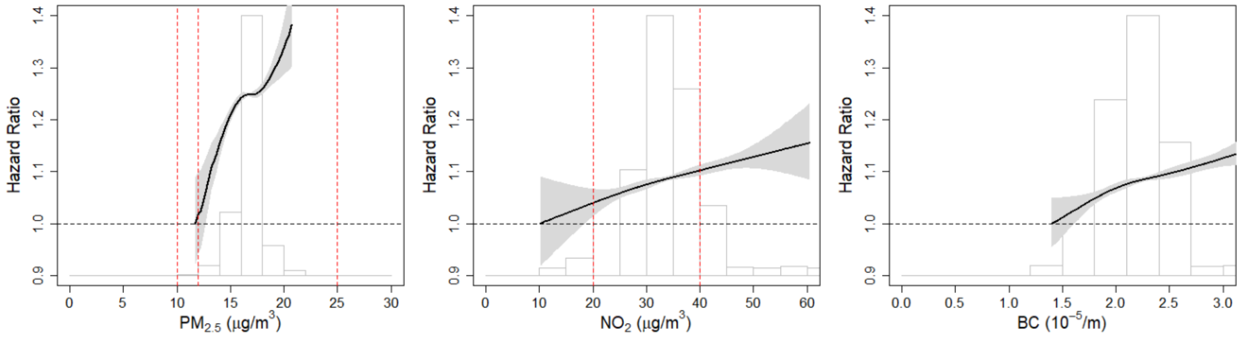
English cohort



Norwegian cohort



Rome cohort



Swiss cohort

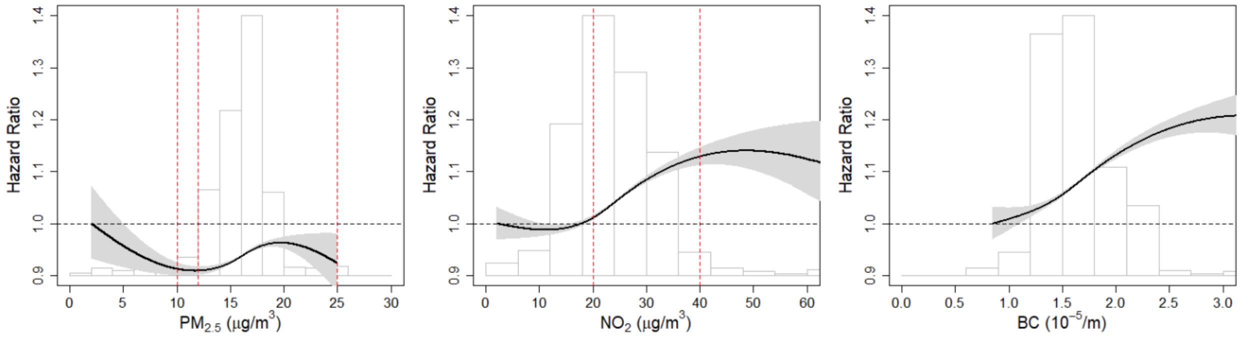
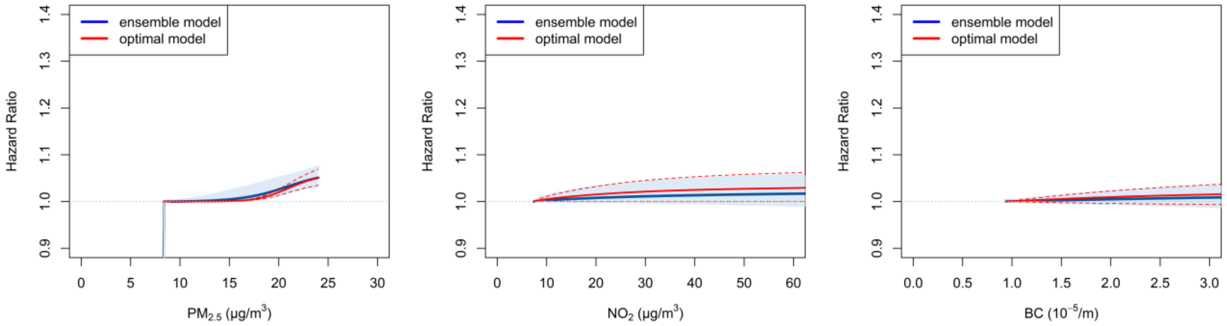
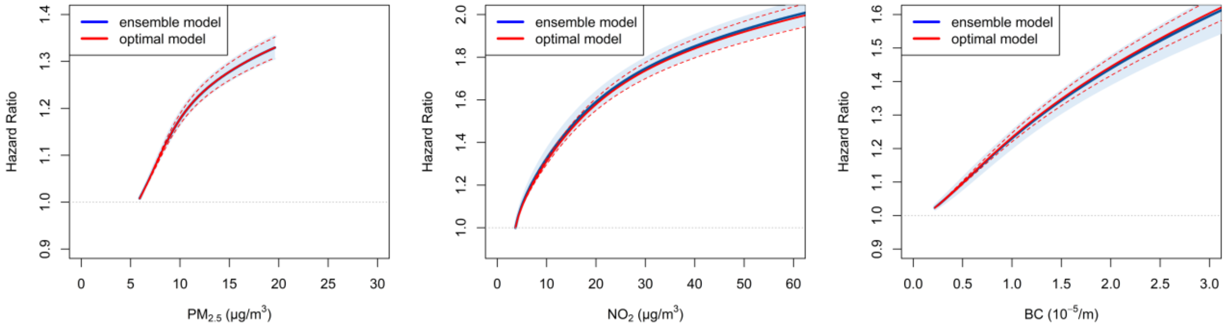


Figure S6. Concentration-response functions of the association between air pollutants and non-accidental mortality in the seven administrative cohorts: air pollutants modelled with Shape-Constrained Health Impact Functions (SCHIF) (light blue regions identify 95% confidence bands)

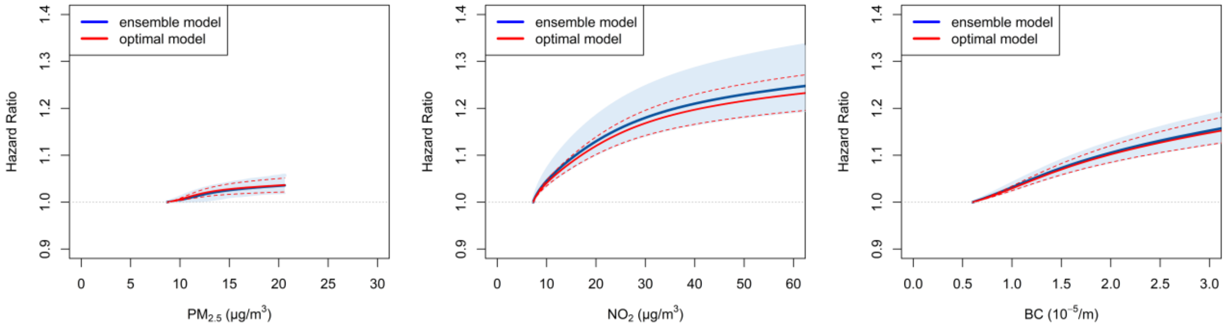
Belgian cohort



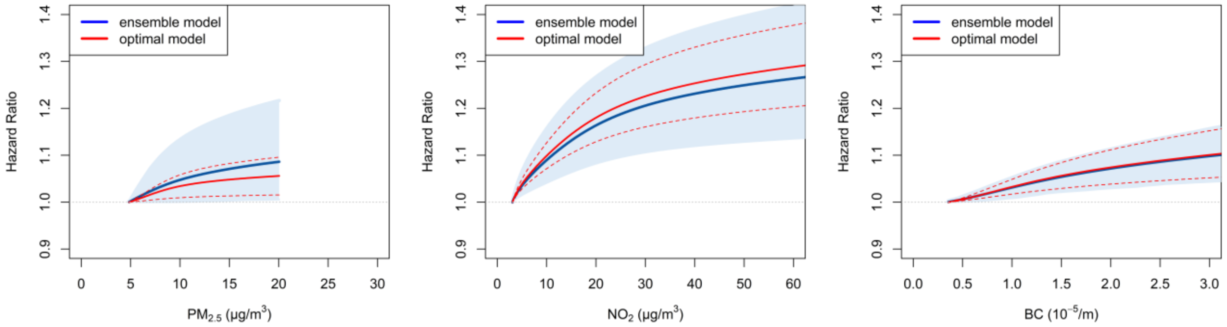
Danish cohort



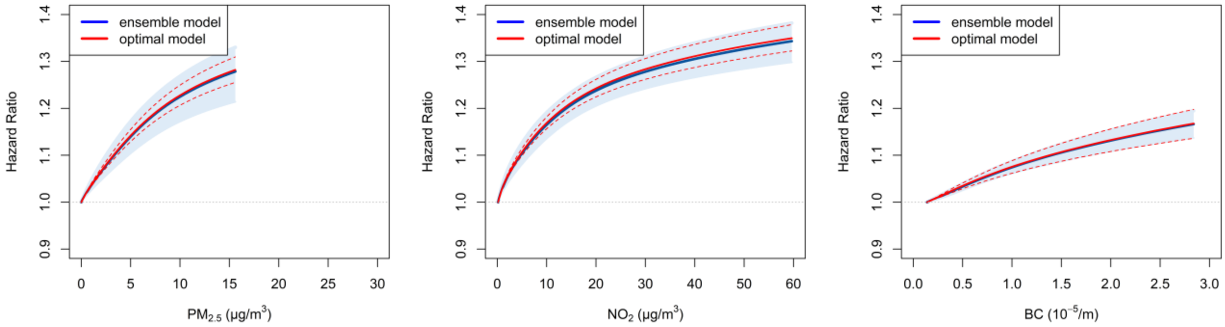
Dutch cohort



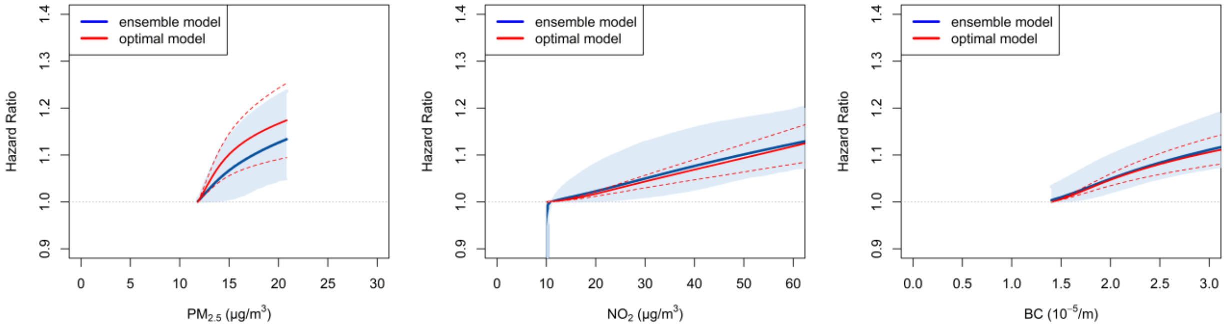
English cohort



Norwegian cohort



Rome cohort



Swiss cohort

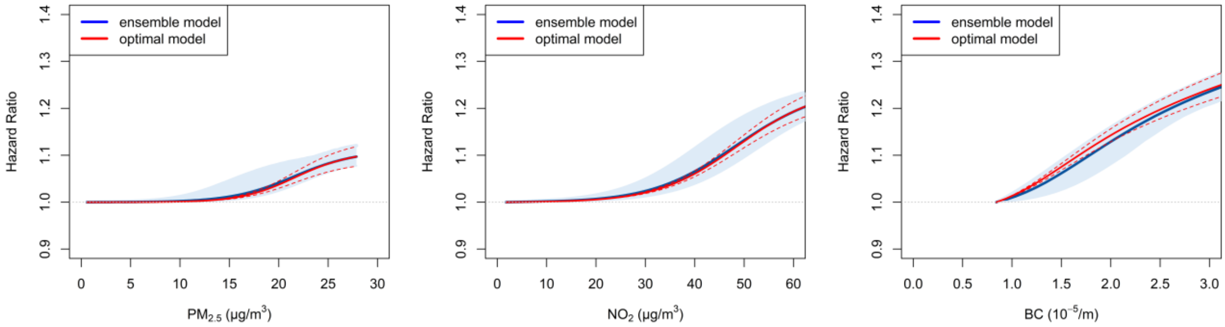


Table S11 reports the meta-analytical results of the subset analysis for cause-specific mortality. Despite the decreasing numbers of subjects and cohorts contributing to the smallest air pollution levels, the associations with mortality remain stable, showing significant harmful effects of all air pollutants on all mortality outcomes even at very low concentrations, i.e. below U.S. EPA standards or WHO guidelines.

Table S11. Association between air pollutants and cause-specific mortality in the subset analysis conducted in seven administrative cohorts: Hazard Ratios (HR), and 95% Confidence Intervals (95% CI) per fixed increments* of the pollutants. Results from the random-effects meta-analysis

Air pollutant	Subset	N. cohorts	N. subjects	Cardiovascular HR (95% CI)	Respiratory HR (95% CI)	Lung cancer HR (95% CI)
PM$_{2.5}$	Full dataset	7	28,146,444	1.041 (1.010, 1.072)	1.064 (1.013, 1.118)	1.102 (1.036, 1.172)
	< 25 µg/m^3	7	28,146,444	1.041 (1.010, 1.072)	1.064 (1.013, 1.118)	1.102 (1.036, 1.172)
	< 20 µg/m^3	7	27,210,961	1.042 (1.012, 1.072)	1.069 (1.015, 1.125)	1.105 (1.036, 1.179)
	< 15 µg/m^3	7	9,703,270	1.044 (0.999, 1.090)	1.063 (0.965, 1.170)	1.115 (1.028, 1.210)
	< 12 µg/m^3	6	4,026,706	1.069 (0.968, 1.182)	1.072 (0.877, 1.312)	1.182 (1.087, 1.285)
	< 10 µg/m^3	4	1,920,292	1.015 (0.993, 1.037)	0.995 (0.782, 1.267)	1.193 (1.144, 1.245)
NO$_2$	Full dataset	7	28,146,444	1.025 (1.006, 1.044)	1.058 (1.024, 1.093)	1.093 (1.053, 1.134)
	< 40 µg/m^3	7	26,085,008	1.030 (1.011, 1.050)	1.069 (1.036, 1.103)	1.102 (1.057, 1.148)
	< 30 µg/m^3	7	16,791,623	1.034 (1.010, 1.059)	1.102 (1.056, 1.149)	1.116 (1.050, 1.185)
	< 20 µg/m^3	7	5,881,351	1.039 (0.979, 1.102)	1.091 (0.951, 1.252)	1.030 (0.813, 1.305)
BC	Full dataset	7	28,146,444	1.022 (1.004, 1.040)	1.053 (1.021, 1.085)	1.078 (1.038, 1.118)
	< 3.0 *10^{-5}/m	7	28,108,712	1.022 (1.004, 1.040)	1.054 (1.023, 1.086)	1.079 (1.039, 1.120)
	< 2.5 *10^{-5}/m	7	27,684,442	1.024 (1.004, 1.045)	1.058 (1.028, 1.090)	1.084 (1.040, 1.129)
	< 2.0 *10^{-5}/m	7	24,278,537	1.024 (1.003, 1.047)	1.066 (1.036, 1.098)	1.079 (1.019, 1.143)
	< 1.5 *10^{-5}/m	6	13,181,589	1.042 (1.014, 1.071)	1.106 (1.038, 1.179)	1.101 (1.041, 1.164)
	< 1.0 *10^{-5}/m	5	4,177,269	1.061 (0.941, 1.195)	1.165 (1.096, 1.238)	1.269 (1.118, 1.440)

Cohort-specific models adjusted for individual-level and area-level confounders available in the administrative cohorts. These include, in almost all cases, age, sex, marital status, educational level, occupational status, individual and area-level income/socio-economic position (details on the cohort-specific confounder models are reported in the supplementary Table S8)

* Fixed increments were: 5 µg/m^3 for PM$_{2.5}$, 10 µg/m^3 for NO$_2$ and 0.5*10-5/m for BC

3.5 Two-pollutant models

The meta-analytical results of the two-pollutant models are reported in Table S12. After adjustment for BC and especially NO_2, $PM_{2.5}$ HRs were attenuated, whereas the HRs for BC and NO_2 remained stable. Two-pollutant models of NO_2 and BC are more difficult to interpret because of the high correlation. In general, NO_2 estimates were robust to BC adjustment, while BC estimates attenuated upon adjustment for NO_2. After adjustment especially for BC and NO_2, the negative associations for O_3 were increased to essentially unity. The attenuation of the $PM_{2.5}$ HR after adjustment for NO_2 was found in most cohorts. Only in the Belgian, Danish and Norwegian a weak association of $PM_{2.5}$ with non-accidental mortality remained. In the other cohorts, the HR was essentially unity with several point estimates below one (data not shown).

For cardiovascular, respiratory and lung cancer mortality, the $PM_{2.5}$ association was also attenuated in two-pollutant models with NO_2. Associations with NO_2 remained in two-pollutant models, especially for lung cancer mortality. Associations with cardiovascular mortality were weakest. Associations with BC remained elevated after adjustment for $PM_{2.5}$, but were strongly reduced after adjustment for NO_2.

Table S12. Association between air pollutants, non-accidental and cause-specific mortality in two-pollutant models from seven administrative cohorts: Hazard Ratios (HR), and 95% Confidence Intervals (95% CI) per fixed increments of the pollutants. Results from the random-effects meta-analysis

Air pollutant	Increment	Single-pollutant HR (95% CI)	Adjusted for PM$_{2.5}$ HR (95% CI)	Adjusted for NO$_2$ HR (95% CI)	Adjusted for BC HR (95% CI)	Adjusted for O$_3$ HR (95% CI)
Non-accidental mortality						
PM$_{2.5}$	5 µg/m^3	1.053 (1.021, 1.085)	-	1.003 (0.982, 1.025)	1.021 (0.997, 1.046)	1.031 (0.999, 1.064)
NO$_2$	10 µg/m^3	1.044 (1.019, 1.069)	1.042 (1.020, 1.065)	-	1.041 (1.009, 1.073)	1.040 (1.012, 1.069)
BC	0.5*10^{-5}/m	1.039 (1.018, 1.059)	1.030 (1.012, 1.049)	1.004 (0.985, 1.022)	-	1.028 (1.005, 1.051)
O$_3$	10 µg/m^3	0.953 (0.929, 0.979)	0.965 (0.942, 0.989)	0.992 (0.968, 1.016)	0.976 (0.948, 1.005)	-
Cardiovascular mortality						
PM$_{2.5}$	5 µg/m^3	1.041 (1.010, 1.072)	-	1.014 (1.003, 1.026)	1.028 (1.009, 1.048)	1.038 (1.014, 1.064)
NO$_2$	10 µg/m^3	1.025 (1.006, 1.044)	1.022 (1.005, 1.040)	-	1.023 (0.997, 1.050)	1.033 (1.013, 1.053)
BC	0.5*10^{-5}/m	1.022 (1.004, 1.040)	1.016 (0.996, 1.037)	1.005 (0.980, 1.031)	-	1.025 (1.005, 1.045)
O$_3$	10 µg/m^3	0.976 (0.954, 0.998)	0.992 (0.970, 1.014)	1.010 (0.988, 1.032)	0.998 (0.977, 1.020)	-
Respiratory mortality						
PM$_{2.5}$	5 µg/m^3	1.064 (1.013, 1.118)	-	1.004 (0.949, 1.062)	1.023 (0.974, 1.075)	1.042 (0.976, 1.112)
NO$_2$	10 µg/m^3	1.058 (1.024, 1.093)	1.053 (1.018, 1.090)	-	1.051 (0.992, 1.112)	1.061 (1.016, 1.108)
BC	0.5*10^{-5}/m	1.053 (1.021, 1.085)	1.042 (1.012, 1.074)	1.009 (0.956, 1.066)	-	1.040 (0.985, 1.099)
O$_3$	10 µg/m^3	0.948 (0.910, 0.988)	0.965 (0.918, 1.014)	1.006 (0.957, 1.057)	0.975 (0.905, 1.051)	-
Lung cancer mortality						
PM$_{2.5}$	5 µg/m^3	1.102 (1.036, 1.172)	-	1.010 (0.948, 1.075)	1.045 (0.986, 1.108)	1.072 (1.006, 1.144)
NO$_2$	10 µg/m^3	1.093 (1.053, 1.134)	1.085 (1.050, 1.120)	-	1.103 (1.056, 1.152)	1.106 (1.065, 1.148)
BC	0.5*10^{-5}/m	1.078 (1.038, 1.118)	1.060 (1.029, 1.091)	0.989 (0.950, 1.030)	-	1.067 (1.029, 1.105)
O$_3$	10 µg/m^3	0.924 (0.887, 0.963)	0.948 (0.914, 0.983)	1.019 (0.971. 1.070)	0.974 (0.936, 1.013)	-

Cohort-specific models adjusted for individual-level and area-level confounders available in the administrative cohorts. These include, in almost all cases, age, sex, marital status, educational level, occupational status, individual and area-level income/socio-economic position (details on the cohort-specific confounder models are reported in the supplementary Table S8)

3.6 Indirect adjustment for smoking and BMI

HRs after indirect adjustment (for non-accidental mortality) are summarized in Table S13. In the Danish, Dutch, Swiss and Norwegian cohorts, HRs were mildly attenuated but remained (borderline) significant. In the Belgian and Rome cohorts, HRs increased after indirect adjustment. In the English cohort indirect adjustment was not necessary, as BMI and smoking data were available for the entire cohort. Table S13 also shows the HRs after adjustment for age-standardized area-level lung cancer, COPD and/or diabetes rates as alternative approaches to adjust for missing lifestyle factors. In the Rome cohort, HRs were moderately attenuated. Overall, associations remained after adjustment for missing lifestyle factors.

Table S13. Association between air pollutants and non-accidental mortality in six administrative cohorts, after indirect adjustment for smoking and body-mass index, or adjustment for area-level lung cancer, COPD or diabetes prevalence rates: Hazard Ratios (HR), and 95% Confidence Intervals (95% CI) per fixed increments* of the pollutants

Air pollutant	Cohort	Main model HR (95% CI)	Indirect adjustment HR (95% CI)	Area-level lung cancer, COPD, diabetes HR (95% CI)
$PM_{2.5}$	Belgian	1.023 (1.011, 1.035)	1.049 (1.036, 1.062)	1.029 (1.017, 1.041) [a]
	Danish	1.141 (1.118, 1.164)	1.118 (1.095, 1.140)	1.143 (1.120, 1.167) [b]
	Dutch	1.021 (0.999, 1.044)	1.015 (0.993, 1.038)	1.007 (0.985, 1.030) [b]
	Norwegian	1.076 (1.066, 1.086)	1.055 (1.045, 1.065)	1.081 (1.067, 1.095) [a,c]
	Rome	1.066 (1.033, 1.099)	1.111 (1.080, 1.142)	1.041 (1.009, 1.075) [b]
	Swiss	1.026 (1.015, 1.038)	1.015 (1.003, 1.027)	Not available
NO_2	Belgian	1.001 (0.995, 1.007)	1.012 (1.006, 1.019)	1.004 (0.998, 1.011) [a]
	Danish	1.107 (1.096, 1.118)	1.088 (1.077, 1.099)	1.107 (1.096, 1.119) [b]
	Dutch	1.030 (1.019, 1.041)	1.020 (1.009, 1.031)	1.024 (1.013, 1.035) [b]
	Norwegian	1.062 (1.055, 1.070)	1.051 (1.044, 1.059)	1.073 (1.063, 1.083) [a,c]
	Rome	1.028 (1.018, 1.038)	1.044 (1.035, 1.053)	1.019 (1.009, 1.029) [b]
	Swiss	1.050 (1.041, 1.059)	1.034 (1.025, 1.042)	Not available
BC	Belgian	1.002 (0.995, 1.008)	1.012 (1.005, 1.019)	1.005 (0.998, 1.012) [a]
	Danish	1.084 (1.073, 1.095)	1.072 (1.061, 1.083)	1.084 (1.073, 1.095) [b]
	Dutch	1.030 (1.019, 1.041)	1.024 (1.013, 1.035)	1.023 (1.012, 1.034) [b]
	Norwegian	1.051 (1.043, 1.059)	1.038 (1.030, 1.046)	1.065 (1.055, 1.076) [a,c]
	Rome	1.031 (1.022, 1.041)	1.037 (1.028, 1.046)	1.022 (1.013, 1.032) [b]
	Swiss	1.057 (1.048, 1.067)	1.037 (1.027, 1.046)	Not available

Cohort-specific models adjusted for individual-level and area-level confounders available in the administrative cohorts. These include, in almost all cases, age, sex, marital status, educational level, occupational status, individual and area-level income/socio-economic position (details on the cohort-specific confounder models are reported in the supplementary Table S8)

* Fixed increments were: 5 μg/m^3 for $PM_{2.5}$, 10 μg/m^3 for NO_2 and O_3, and 0.5*10-5/m for BC

[a] Municipality-level diabetes and lung cancer simultaneously

[b] Regional scale lung cancer and diabetes simultaneously

[c] The adjustment of area-level lung cancer and diabetes used a reduced population N=1,868,397 compared to N=2,309,001 for the main model and the indirect adjustment.

3.7 Results of the sensitivity analysis

Tables S14-S16 summarize the results of the sensitivity analysis on use of back-extrapolated exposures at baseline (Table S14), time-varying analyses (Table S15 and Figure S7) and adjustment for road traffic noise (Table S16).

The combined HRs were almost identical to the HR in the main model for the baseline exposure back-extrapolated with the difference method (Table S14). The HRs for the baseline exposure back-extrapolated with the ratio method were slightly smaller than for the main exposure for $PM_{2.5}$ and NO_2 and almost identical for BC and O_3, probably reflecting the smaller time trends for the latter pollutants. The confidence intervals were smaller for the ratio-baseline exposure reflecting the larger variability in exposure and the reduced heterogeneity in effect estimates across cohorts (data not shown).

Table S14. Association between air pollutants and non-accidental mortality in seven administrative cohorts, from models using back-extrapolated exposures at baseline, with either the "difference" or the "ratio" methods: Hazard Ratios (HR), and 95% Confidence Intervals (95% CI) per fixed increments* of the pollutants, results from the random-effects meta-analysis

Air pollutant	Main model HR (95% CI)	Back-extrapolation, difference method HR (95% CI)	Back-extrapolation, ratio method HR (95% CI)
$PM_{2.5}$	1.053 (1.021, 1.085)	1.051 (1.018, 1.085)	1.039 (1.018, 1.061)
NO_2	1.044 (1.019, 1.069)	1.044 (1.020, 1.069)	1.036 (1.018, 1.055)
BC	1.039 (1.018, 1.059)	1.039 (1.019, 1.059)	1.038 (1.017, 1.058)
O_3 (warm season)	0.953 (0.929, 0.979)	0.953 (0.929, 0.978)	0.953 (0.930, 0.976)

Cohort-specific models adjusted for individual-level and area-level confounders available in the administrative cohorts. These include, in almost all cases, age, sex, marital status, educational level, occupational status, individual and area-level income/socio-economic position (details on the cohort-specific confounder models are reported in the supplementary Table S8)

* Fixed increments were: 5 μg/m^3 for $PM_{2.5}$, 10 μg/m^3 for NO_2 and O_3, and 0.5*10-5/m for BC

Meta-analytical HRs for time-varying exposures with 1-year strata to adjust for time trends are displayed in Table S15. In general, we found a negligible attenuation of the air pollutants-mortality associations compared to either the main analysis (Table 2) or the one conducted with baseline back-extrapolated exposures (Table S14). When air pollutants were entered with natural splines (Figure S7), we confirmed the increasing or supra-linear associations detected in the main analysis (Figures 3 and S5), with large differences among cohorts.

Table S15. Association between air pollutants and non-accidental mortality in seven administrative cohorts, from time-varying models with 1-yr strata adjustment for time trends: Hazard Ratios (HR), and 95% Confidence Intervals (95% CI) per fixed increments* of the pollutants, results from the random-effects meta-analysis

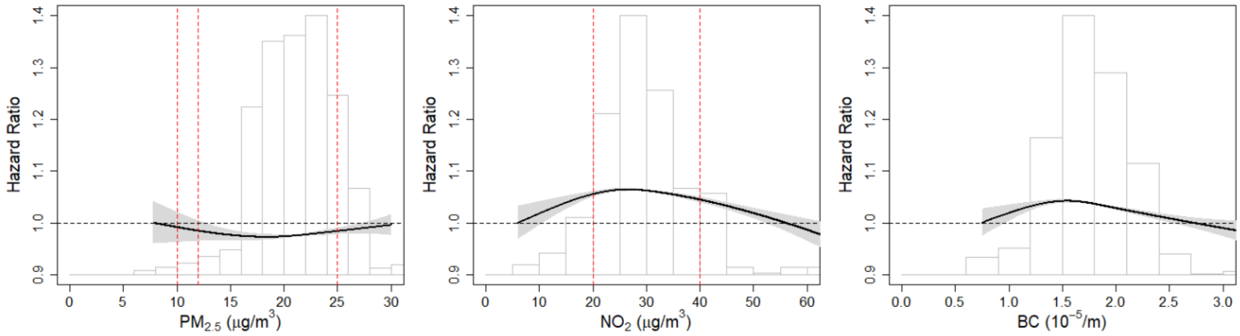
Air pollutant	Main model HR (95% CI)	Time-varying analysis, difference method HR (95% CI)	Time-varying analysis, ratio method HR (95% CI)
$PM_{2.5}$	1.053 (1.021, 1.085)	1.047 (1.012, 1.083)	1.039 (1.012, 1.068)
NO_2	1.044 (1.019, 1.069)	1.039 (1.014, 1.063)	1.037 (1.014, 1.060)
BC	1.039 (1.018, 1.059)	1.033 (1.014, 1.052)	1.034 (1.015, 1.054)
O_3 (warm season)	0.953 (0.929, 0.979)	0.957 (0.932, 0.982)	0.958 (0.934, 0.983)

Cohort-specific models adjusted for individual-level and area-level confounders available in the administrative cohorts. These include, in almost all cases, age, sex, marital status, educational level, occupational status, individual and area-level income/socio-economic position (details on the cohort-specific confounder models are reported in the supplementary Table S8). Time-varying models run on expanded datasets with individual follow-up times split by year, and adjustment of years of follow up as a strata term.

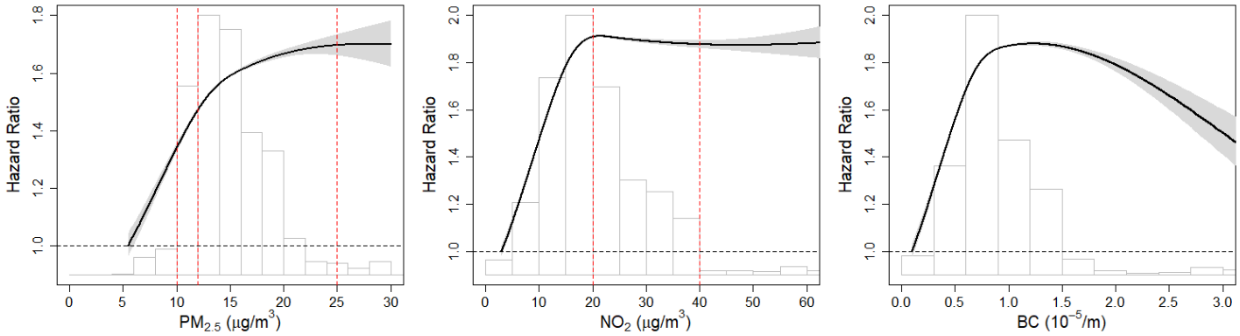
* Fixed increments were: 5 $\mu g/m^3$ for $PM_{2.5}$, 10 $\mu g/m^3$ for NO_2 and O_3, and 0.5*10-5/m for BC

Figure S7. Concentration-response functions of the association between air pollutants and non-accidental mortality in the seven administrative cohorts, from time-varying models with 1-yr strata adjustment for time trends: air pollutants modelled with natural splines with 3 degrees of freedom (grey regions identify 95% confidence bands)

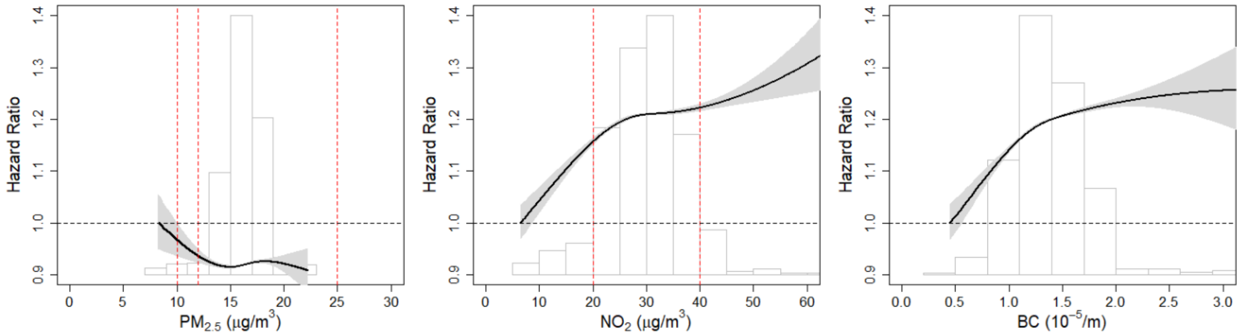
Belgian cohort



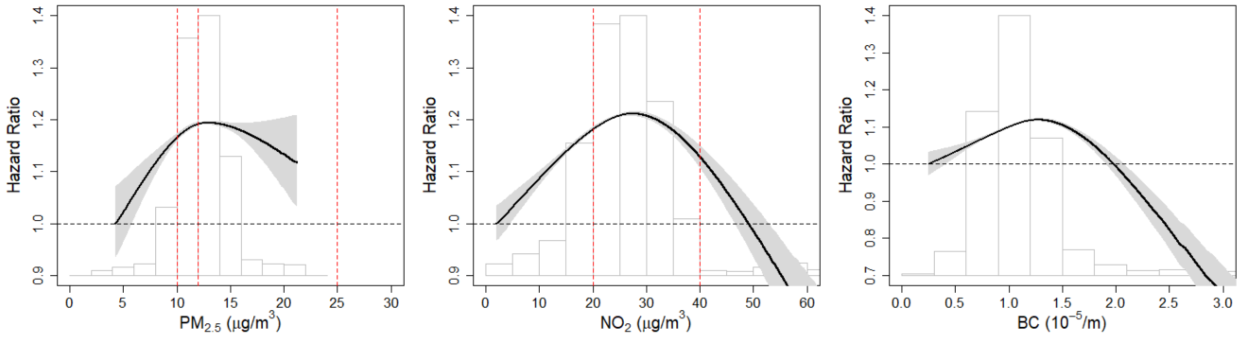
Danish cohort



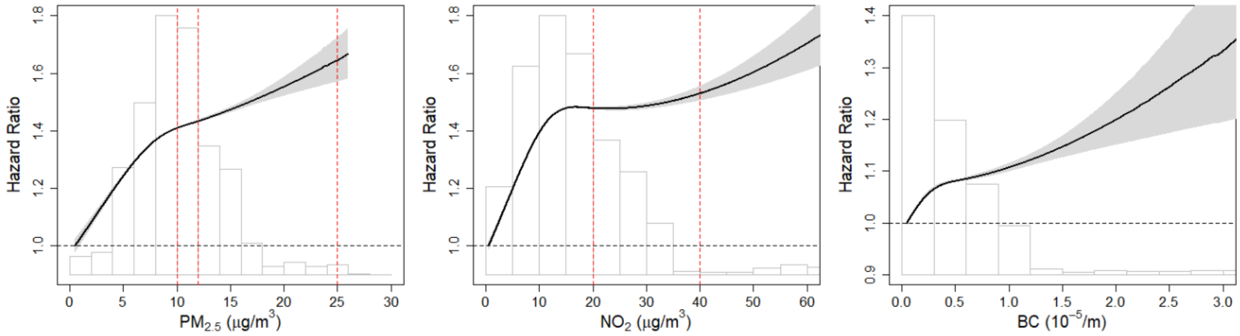
Dutch cohort



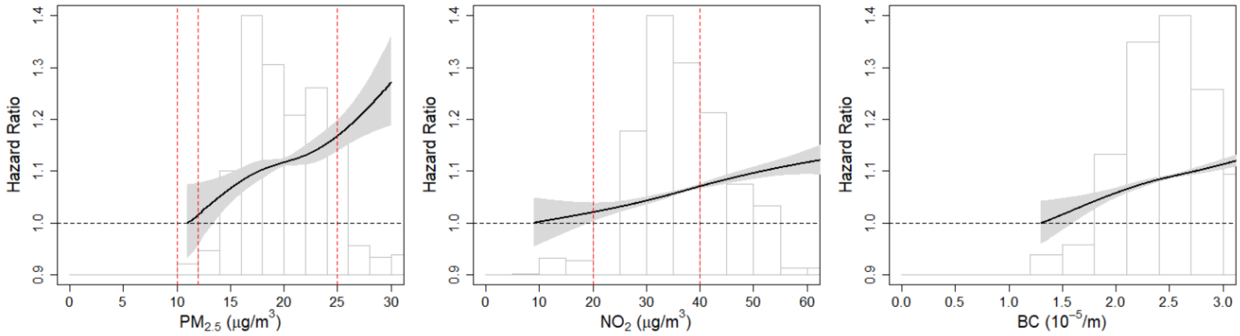
English cohort



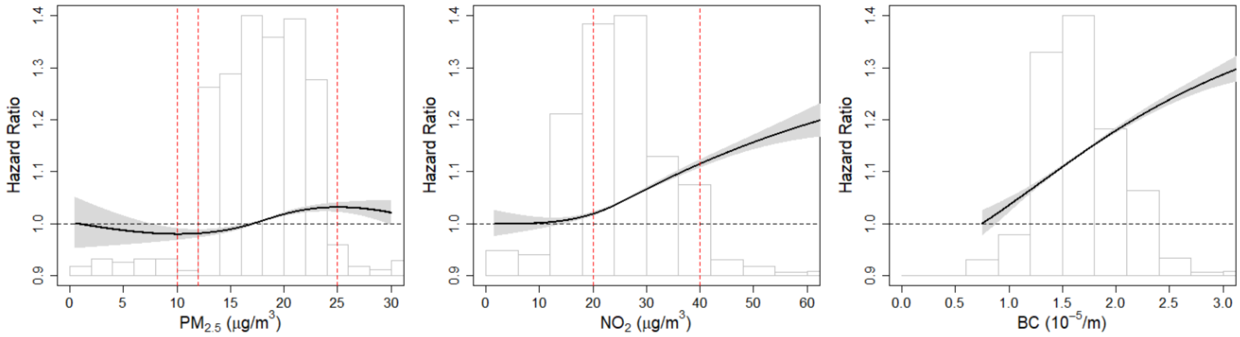
Norwegian cohort



Rome cohort



Swiss cohort



Finally, results of the models adjusted for road traffic noise are reported in Table S16. Further adjustment of the cardiovascular mortality associations for traffic noise did not result in substantial changes of the air pollution effect estimates in the Dutch, Norwegian and Rome cohorts. In the Swiss cohort, associations were attenuated substantially, with only a borderline significant association for BC remaining. In the Belgian cohort, HRs were not affected by further adjustment for noise, but noise exposure assessment was only possible for the Brussels capital area. HRs in this strongly reduced population differed from the full cohort (data not shown), so the Belgian cohort noise adjustment results need to be interpreted with caution.

Table S16. Association between air pollutants and cardiovascular mortality in five administrative cohorts, from models adjusted for road traffic noise: Hazard Ratios (HR), and 95% Confidence Intervals (95% CI) per fixed increments* of the pollutants, cohort-specific results

Air pollutant	Cohort	Main model HR (95% CI)	Adjustment for noise HR (95% CI)
$PM_{2.5}$	Belgian	1.001 (0.983, 1.020)	0.978 (0.890, 1.075)
	Dutch	1.015 (0.988, 1.042)	1.022 (0.994, 1.050)
	Norwegian	1.044** (1.026, 1.063)	1.035** (1.017, 1.054)
	Rome	1.109 (1.058, 1.162)	1.077 (1.023, 1.134)
	Swiss	1.026 (1.008, 1.044)	1.012 (0.994, 1.031)
NO_2	Belgian	0.989 (0.980, 0.998)	0.982 (0.952, 1.013)
	Dutch	1.017 (1.003, 1.031)	1.029 (1.014, 1.044)
	Norwegian	1.036** (1.023, 1.049)	1.030** (1.016, 1.043)
	Rome	1.044 (1.027, 1.061)	1.036 (1.018, 1.055)
	Swiss	1.026 (1.014, 1.039)	1.004 (0.991, 1.017)
BC	Belgian	0.984 (0.973, 0.994)	0.997 (0.963, 1.032)
	Dutch	1.018 (1.003, 1.033)	1.030 (1.014, 1.046)
	Norwegian	1.024** (1.011, 1.037)	1.016** (1.002, 1.030)
	Rome	1.043 (1.026, 1.060)	1.032 (1.015, 1.050)
	Swiss	1.036 (1.022, 1.051)	1.014 (0.999, 1.029)

Cohort-specific models adjusted for individual-level and area-level confounders available in the administrative cohorts. These include, in almost all cases, age, sex, marital status, education level, occupational status, individual or area-level income/socio-economic position.

* Fixed increments were: 5 $\mu g/m^3$ for $PM_{2.5}$, 10 $\mu g/m^3$ for NO_2 and O_3, and 0.5*10-5/m for BC

** The adjustment of noise used a reduced population N=1,824,283 compared to N=2,309,001 for the main model.

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