Supplement material

Long-term exposure to low-level air pollution and incidence of asthma: the ELAPSE project

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1. Description of the Three Study Cohorts.

We included three out of 11 pooled ELAPSE large prospective cohorts into our analyses. One of the cohorts, the CEANS cohort, is composed of four individual Swedish cohorts. The other two study cohorts, the DCH cohort and the DNC cohort, are from Denmark. The DNC cohort includes two parts of participants who were recruited in 1993 or 1999.

1) CEANS, Cardiovascular Effects of Air Pollution and Noise, Sweden: including SDPP, SIXTY, SALT, and SNAC-K.

SDPP, the Stockholm Diabetes Preventive Program (SDPP), Sweden

The Stockholm diabetes prevention program was a population-based prospective study and aimed at investigating the etiology of type 2 diabetes and developing prevention strategies for type 2 diabetes [1]. An initial survey included all men and women in the targeted age group in Stockholm County; for men in four municipalities (Värmdö, Upplands Bro, Tyresö and Sigtuna), and for women these four plus a fifth municipality (Upplands Väsby). All were screened by a questionnaire regarding presence of own diabetes and diabetes in relatives. Subjects with family history of diabetes (FHD) and randomly selected subjects without FHD, all without previously diagnosed diabetes, were invited to a health examination. This baseline study, 1992−1994 for men and 1996−1998 for women, comprised 7,949 subjects, aged 35−56 years, and about 50% had FHD. In the follow-up study 8−10 years later, 2,383 men (2002–2004) and 3,329 women (2004–2006) participated. At the health examinations, both at baseline and follow-up, an extensive questionnaire (information on lifestyle factors, such as physical activity, dietary habits, tobacco use, alcohol consumption, health status, socioeconomic status and psychosocial conditions) was completed. Diabetes heredity was confirmed and measurements of weight, height, hip and waist circumference as well as blood pressure were performed. In addition, an oral glucose tolerance test (OGTT) was made, and blood was sampled at fasting state and 2 hour after glucose intake. Outcomes based on the

Swedish nationwide health registries (such as the myocardial infarction and stroke registries, the cause-of death register, and the national patient register) have been used.

SIXTY, the Cohort of 60-year-olds, Sweden

The Cohort of 60-year-olds is a study aiming to identify biological and socio-economic risk factors and predictors for cardiovascular diseases [2]. Recruitment took place between August 1997 and March 1999. A random sample of every third man and woman living in Stockholm County, who was born between 1 July 1937 and 30 June 1938, was invited to participate. In total, 4,232 subjects were included. Height, weight, BMI, Waist/Hip ratio and resting ECD, blood pressure and fasting blood samples were taken during a physical examination, while a comprehensive questionnaire was completed, including information on socioeconomic, medical and life-style factors. Outcomes based on the Swedish nationwide health registries (such as the myocardial infarction and stroke registries, the cause-of-death register and the national patient register) have been used.

SALT, the Stockholm Screening Across the Lifespan Twin study, Sweden

Participants come from two sub-studies of the Swedish Twin Registry (STR) [3]. The Screening Across the Lifespan Twin study (SALT) [4] & TwinGene [5] was set-up to screen all twins born in Sweden before 1958 for the most common complex diseases with a focus on cardiovascular diseases. TwinGene is a sub-study establishing a biobank with DNA and serum from SALT participants. SALT is based on a telephone interview and recruitment took place between 1998 and 2002. Information concerning birth order and weight, zygosity, contact with twin partner and family constellation, diseases, use of medication, occupation, education, life style habits, gender- and age specific (hormone replacement therapy) and memory problems (age > 65) was collected. In TwinGene, twins born before 1958 were contacted 2004-2008. Health and medication data were collected from questionnaires. Blood sampling material was mailed to study subjects, who contacted a local health care center for blood sampling. Information about COPD come from linkages to Swedish nationwide health registries. This investigation on air pollution is restricted to participants living in Stockholm County.

SNAC-K, The Swedish National study of Aging and Care in Kungsholmen, Sweden

SNAC-K is an ongoing longitudinal study aiming to investigate the ageing process and identify possible preventive strategies to improve health and care in elderly adults [6]. The study population consists of randomly sampled individuals >=60 years old and in a central area of Stockholm (Kungsholmen) between March 2001 and June 2004. The sample was stratified for age and year of assessment giving sub-cohorts with 60, 66, 72, 78, 81, 84, 87, 90, 93, 96, and 99+ year olds. Information was collected through social interviews, assessment of physical functioning, clinical examination (incl. geriatric, neurological and physical assessments) as well as cognitive assessment. At baseline, information regarding events prior to the study period was gathered. The follow-up interval is six years for the younger age cohorts, and three years for the older age cohorts (81+). During the follow-up intervals, medical events of all participants are registered through linkage with primary care registry and hospital discharge registry (available for all subjects in Sweden). In case of death, hospital and cause of death registries provide the clinical information, and informant interviews are carried out. The same protocol as for the baseline data collection is used during the follow-up, though only concerning the follow-up period. Website of study: https://www.snac-k.se. Any outcomes based on the Swedish nationwide health registries (such as the myocardial infarction and stroke registries, the cause-of-death register and the national patient register) have been used.

2) DCH, Danish Diet, Cancer and Health study, Denmark

The primary aim of the DCH study is to investigate diet and lifestyle in relation to incidence of cancer and other chronic diseases [7]. Historical residential history of the study participants is available, which facilitate studies of air pollution and noise. The study enrolled participants in two areas, Copenhagen and Aarhus, Denmark. 160,725 individuals aged 50–64 years were invited to participate between December 1993 and May 1997. Out of the 160,725 people invited, 57,053 were enrolled. On enrolment, each participant completed self-administered questionnaires (in Danish) that included questions on dietary habits, health status, family history of cancer, social factors, reproductive factors, smoking, environmental smoking, and lifestyle habits. Anthropometric measurements including blood pressure and blood samples were also obtained. The DCH cohort is followed up regularly by use of complete nationwide registers hence the loss to follow-up is virtually nil. Data on asthma incidence from the Danish National Patient Registry were used.

3) DNC, Danish Nurse Cohort study, Denmark

The Danish Nurse Cohort was established in 1993 and includes a total of 28,731 female members of the Danish Nurse Organization who were 44 years of age or older at recruitment in 1993 or 1999 [8]. Inspired by the American Nurses' Health Study, the Danish Nurse Cohort aimed to provide the basis for research into the potential health effects related to use of hormone replacement therapy (HRT) in a European population. In 1993, the cohort was initiated by sending a questionnaire to 23,170 female members of the Danish Nurse Organization who were at least 44 years old at the time. The Danish Nurse Organization includes 95% of all nurses in Denmark. In total, 19,898 nurses accepted an invitation and answered a comprehensive questionnaire on lifestyle (smoking, alcohol consumption, leisure time physical activity, diet, BMI, etc.), occupational characteristics (shift work, work environment, etc.), health, reproductive factors, and other factors. The cohort was reinvestigated in 1999, adding 8,833 nurses (8,344 new nurses who turned 44 in the period 1993–1999 and 489 non-responders from the 1993 who were re-invited).

2. Air Pollution Exposure Assessment

Annual average concentrations of $PM_{2.5}$, NO_2, BC, and warm season O_3 (April through September; the maximum running 8-hour averages) for 2010 were estimated at the study participants' baseline residential addresses with the use of standardized Europe-wide hybrid land use regression (LUR) models [9, 10]. The LUR models incorporated the European Environment Agency (EEA) AirBase routine monitoring data for $PM_{2.5}$, NO_2, and O_3 and ESCAPE monitoring data for BC. BC was measured by the reflectance of $PM_{2.5}$ filters and expressed in absorbance units [9]. Satellite and chemical transport model air pollution estimates, land use, and traffic data were predictors to develop models for annual mean air pollution concentrations. The developed hybrid LUR models were used to create exposure surfaces at a 100 × 100 m spatial scale for exposure assignments to the cohorts. The exposure models performed well in five-fold hold-out validation, explaining a large fraction of spatial variability for $PM_{2.5}$ (72%), NO_2 (59%), BC (54%), and O_3 (69%) in the measured annual mean concentrations [9]. Additionally, predictions from the 2010 model correlated highly with models developed for 2000 and 2005 models for (NO_2 and O_3) and 2013 model for $PM_{2.5}$ at the overall European scale, with squared correlations (R^2) larger than 76% [9].

We also estimated pollutant concentrations for each year from recruitment to the end of follow-up using back-extrapolation to 1990. We back-extrapolated by using a chemical transport and dispersion model, the Danish Eulerian Hemispheric Model (DEHM) [11], which calculated monthly average concentrations across Europe at 26 × 26 km resolution. The rationale to use DEHM for back-extrapolation is the consistent availability of estimates across Europe for the full study period for all pollutants. In contrast, routine monitoring data were less consistent, not available for BC and only available from about 2008 for $PM_{2.5}$. Residential address histories for each year were incorporated in the back-extrapolation, such that both changes in air pollution spatial patterns and moving residential address were accounted for. For application to the cohorts, we calculated population weighted average concentrations at the study area level, allowing different spatial trends within Europe. We back-extrapolated concentrations for all pollutants using both an absolute difference and a ratio method with 2010 as the reference. With the absolute 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. In case of higher concentrations in the past, the ratio method therefore increases the contrast in cohort exposures.

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Table S1. Overview of studies on air pollution and asthma incidence in adults.

Author, year	Cohort/Study	Sample Size (N)	Asthma incidence defintion	Pollutant (mean levels)	Effect estimates
McDonnell et al., 1999 [12]	The Ahsmog Study, California, USA,	3,091 non-smokers	Self-reported asthma diagnosed by a doctor	O_3 (46.5 ppb)	RR (95% CI): M: 2.09 (1.03–4.16) per 27 ppb F: 0.86 (0.58–1.26) per 27 ppb
Jacquemin et al., 2009 [13]	European Respiratory Health Survey (ECRHS), 17 European cities	4,185	Self-reported ever asthma diagnosed by a doctor	NO_2 (median: 27.7 $\mu g/m^3$)	OR (95% CI): 1.43 (1.02–2.01) per 10 $\mu g/m^3$
Künzli et al., 2009 [14]	The SAPALDIA cohort, Switzerland	2,725 never-smokers	Self-reported doctor-diagnosed asthma	$dTPM_{10}$ (-0.59 $\mu g/m^3$)	HR (95% CI): 1.30 (1.05–1.61) per 1 $\mu g/m^3$
Modig et al., 2009 [15]	The Respiratory Health in Northern Europe (RHINE) cohort, Sweden	3,609	Self-reported asthma with questionnaire	NO_2 (17.9 $\mu g/m^3$)	OR (95% CI): 1.54 (1.00–2.36) per 10 $\mu g/m^3$
Andersen et al., 2012 [16]	The Diet, Cancer and Health cohort, Denmark	57,053	Hospital contact (in-, outpatient, or emergency) primary discharge diagnoses ICD-10: J45–46	NO_2 (median: 15.2 $\mu g/m^3$)	HR (95% CI): 1.10 (1.01–1.20) per 5.8 $\mu g/m^3$

Young et al., 2014 [17]	The Sister Study, USA	50,884 women (sisters with breast cancer)	Self-reported doctor diagnosed asthma	NO_2 (median: 9.3 ppb) $PM_{2.5}$ (median 10.8 μg/m^3)	OR (95% CI): 1.12 (0.96–1.30) per 5.8 ppb 1.20 (0.99–1.46) per 3.6 μg/m^3
Jacquemin et al., 2015 [18]	The European Study of Cohorts for Air Pollution Effects (ESCAPE), six cohorts	23,704 adults	Self-reported ever asthma diagnosed by a doctor, breathless while wheezing, asthma attacks, or asthma medication	NO_2 (mean range 22–31 μg/m^3 by cohort) $PM_{2.5}$ (mean range 10–18 μg/m^3 by cohort) $PM_{2.5absorbance}$ (mean range 1.0–2.1 $10^{-5}m^{-1}$ by cohort)	OR (95% CI): 1.10 (0.99–1.21) per 10 μg/m^3 1.04 (0.88–1.23) per 5 μg/m^3 1.06 (0.95–1.19) per 1 $10^{-5}m^{-1}$
Fisher et al., 2016 [19]	The Nurses' Health Study, USA	121,701 female nurses	Self-reported physician-diagnosed asthma and use of asthma medication	$PM_{2.5}$ (14.2 μg/m^3)	HR (95% CI): 0.90 (0.73–1.12) per 10 μg/m^3
Weichenthal et al., 2017 [20]	The Ontario Population Health and Environment Cohort (ONPHEC), Toronto Canada,	1,100,000	Ontario Asthma Surveillance System (physician insurance	NO_2 (21.4 ppb) $PM_{2.5}$ (10.9 μg/m^3) UFPs (28,473 count/cm^3)	HR (95% CI): 1.03 (1.02–1.05) per 4.1 ppb 1.02 (1.00–1.04) per 3.2 μg/m^3

			claims, hospital admissions and medication data): ICD-9: 493		1.00 (1.00–1.01) per 10,097 count/cm^3
Salimi et al., 2018 [21]	The Sax Institute's 45 and Up Study, Sydney, Australia	100,084	Primary diagnosis of hospitalization ICD-10: J45–46	NO_2 (17.5 μg/m^3) $PM_{2.5}$ (4.5 μg/m^3)	HR (95% CI): 1.03 (0.88–1.19) per 5 μg/m^3 1.08 (0.89–1.30) per 1 μg/m^3

$PM_{2.5}$, particulate matter with diameter < 2.5 μm; $dTPM_{10}$, the difference in traffic-related particulate matter with diameter < 10 μm; NO_2, nitrogen dioxide; BC, black carbon; O_3, ozone; HR, hazard ratio; OR, odds ratio; CI, confidence interval; SAPALDIA, The Swiss Cohort Study on Air Pollution and Lung Diseases in Adults;

Unit conversion for pollutant concentration, for NO_2: 1 ppb = 1.88 μg/m^3; for O_3: 1 ppb = 2.00 μg/m^3.

Table S2. Characteristics of participants by cohorts and adult-onset asthma status at baseline based on the number of observations in Model 3

Characteristic at baseline*	All cohorts (N=98,326)			DCH (N=52,961)			DNC (N=24,978)					
							1993 (N=16,937)			1999 (N=8,041)		
	Total	No asthma	Asthma	Total	No asthma	Asthma	Total	No asthma	Asthma	Total	No asthma	Asthma
Baseline period	1992–2004			1993–1997			1993			1999		
End of follow-up	2011, 2015			2015			2015			2015		
Person-years at risk, N	1,634,458	1,601,795	32,664	928,404	918,007	10,397	327,563	324,095	3,468	126,658	125,361	1,298
Follow-up time, years (Mean ± SD)	16.6±5.2	16.8±5.0	8.9±5.8	17.5±4.7	17.7±4.5	9.1±5.9	19.3±5.6	19.5±5.4	9.9±6.6	15.8±2.4	15.9±2.1	8.7±5.0
Number of observations	98,326	96,361	1,965	52,961	51,813	1,148	16,937	16,585	352	8,041	7,892	149
Asthma incidence rate	2.0%			2.2%			2.1%			1.9%		
Age, years (Mean ± SD)	55.8±7.5	55.8±7.5	55.4±6.7	56.6±4.4	56.6±4.4	56.8±4.4	56.2±8.4	56.2±8.4	54.2±7.6	47.9±4.2	47.9±4.2	47.9±3.7
Age categories, N (%)												
< 65 years old	91,318 (93)	89,462 (93)	1,856 (94)	52,335 (99)	51,203 (99)	1,132 (99)	14,318 (85)	14,002 (84)	316 (90)	7,914 (98)	7,767 (98)	147 (99)
≥ 65 years old	7,008 (7)	6,899 (7)	109 (6)	626 (1)	610 (1)	16 (1)	2,619 (15)	2,583 (16)	36 (10)	127 (2)	125 (2)	2 (1)

Female, N (%)	64,492 (66)	63,073 (65)	1,419 (72)	27,732 (52)	27,023 (52)	709 (62)	16,937 (100)	16,585 (100)	352 (100)	8,041 (100)	7,892 (100)	149 (100)
BMI, kg/m^2 (Mean ± SD)	25.3±4.0	25.3±4.0	25.9±4.4	26.0±4.1	26.0±4.1	26.4±4.3	23.6±3.5	23.6±3.4	24.3±4.2	23.9±3.6	23.9±3.6	24.6±3.9
BMI, WHO categories, N (%)												
<18.5	1,298 (1)	1,273 (1)	25 (1)	416 (1)	404 (1)	12 (1)	495 (3)	484 (3)	11 (3)	139 (2)	138 (2)	1 (1)
18.5–24.9	49,901 (51)	49,007 (51)	894 (45)	22,893 (43)	22,436 (43)	457 (40)	11,688 (69)	11,467 (69)	221 (63)	5,492 (68)	5,400 (68)	92 (62)
25.0–29.9	35,604 (36)	34,867 (36)	737 (38)	22,013 (42)	21,536 (42)	477 (42)	3,875 (23)	3,790 (23)	85 (24)	1,875 (23)	1,832 (23)	43 (29)
≥30.0	11,523 (12)	11,214 (12)	309 (16)	7,639 (14)	7,437 (14)	202 (18)	879 (5)	844 (5)	35 (10)	535 (7)	522 (7)	13 (9)
Smoking status, N (%)												
Current smoker	32,398 (33)	31,842 (33)	556 (28)	19,218 (36)	18,869 (36)	349 (30)	6,357 (38)	6,247 (38)	110 (31)	2,303 (29)	2,263 (29)	40 (27)
Previous smoker	29,533 (30)	28,884 (30)	649 (33)	14,728 (28)	14,371 (28)	357 (31)	4,824 (28)	4,711 (28)	113 (32)	2,619 (33)	2,567 (33)	52 (35)

Never smoker	36,395 (37)	35,635 (37)	760 (39)	19,045 (36)	18,573 (36)	442 (39)	5,756 (34)	5,627 (34)	129 (37)	3,119 (39)	3,062 (39)	57 (38)
Smoking duration, years (Mean ± SD)	17.1±16.5	17.1±16.5	16.1±16.0	19.1±17.2	19.1±17.2	17.7±16.7	16.5±15.8	16.5±15.8	14.6±15.1	12.5±12.7	12.5±12.7	12.8±12.9
Smoking intensity, n/day (Mean ± SD)	9.2±10.4	9.2±10.4	8.9±10.3	10.4±11.2	10.5±11.3	9.4±10.6	8.4±9.3	8.4±9.3	7.8±9.3	7.5±8.4	7.5±8.3	9.5±11.1
Marital status, N (%)												
Single	8,450 (9)	8,298 (9)	152 (8)	3,194 (6)	3,138 (6)	56 (5)	1,782 (11)	1,757 (11)	25 (7)	749 (9)	735 (9)	14 (9)
Married or living with partner	70,137 (71)	68,790 (71)	1,347 (69)	37,928 (72)	37,130 (72)	798 (70)	11,471 (68)	11,235 (68)	236 (67)	6,105 (76)	6,001 (76)	104 (70)
Divorced/Separated	13,755 (14)	13,413 (14)	342 (17)	8,917 (17)	8,694 (17)	223 (19)	2,098 (12)	2,039 (12)	59 (17)	1,024 (13)	997 (13)	27 (18)
Widowed	5,984 (6)	5,860 (6)	124 (6)	2,922 (6)	2,851 (6)	71 (6)	1,586 (9)	1,554 (9)	32 (9)	163 (2)	159 (2)	4 (3)
Employment status, N (%)												
Employed	75,111 (76)	73,616 (76)	1,495 (76)	41,519 (78)	40,650 (78)	869 (76)	11,877 (70)	11,609 (70)	268 (76)	7,621 (95)	7,477 (95)	144 (97)

Others	23,215 (24)	22,745 (24)	470 (24)	11,442 (22)	11,163 (22)	279 (24)	5,060 (30)	4,976 (30)	84 (24)	420 (5)	415 (5)	5 (3)
Educational levels, N (%)*												
Low level	14,102 (14)	13,845 (14)	257 (13)	7,819 (15)	7,644 (15)	175 (15)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Medium level	40,914 (42)	40,031 (42)	883 (45)	33,404 (63)	32,644 (63)	760 (66)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
High level	43,310 (44)	42,485 (44)	825 (42)	11,738 (22)	11,525 (22)	213 (19)	16,937 (100)	16,585 (100)	352 (100)	8,041 (100)	7,892 (100)	149 (100)
COPD, N (%)#	485 (0.5)	474 (0.5)	11 (1)	365 (1)	320 (1)	45 (4)	60 (0.4)	53 (0.3)	7 (2)	14 (0.2)	14 (0.2)	0 (0)
Area-level mean year incomeϕ	20991.8	20994.5	20857.3	20199.0	20193.7	20436.8	19229.3	19226.4	19366.9	18983.3	18980.8	19113.6

Table S2 continued.

Characteristic at baseline*	**CEANS (N=20,387)**											
	SDPP (N=7,520)			**SIXTY (N=3,931)**			**SALT (N=6,128)**			**SNAC-K (N=2,808)**		

	Total	No asthma	Asthma	Total	No asthma	Asthma	Total	No asthma	Asthma	Total	No asthma	Asthma
Enrollment period		1992–1998			1997–1999			1998–2002			2001–2004	
End of follow-up		2011			2011			2011			2011	
Person-years at risk, N	118,408	117,103	1,305	50,027	49,552	475	62,880	62,464	416	20,519	20,339	180
Follow-up time, years (Mean ± SD)	15.7±2.6	15.9±2.4	9.8±4.2	12.7±2.6	12.8±2.5	6.7±3.8	10.3±2.5	10.3±2.4	5.3±3.3	7.3±2.9	7.3±2.9	5.5±2.5
Number of observations	7,520	7,387	133	3,931	3,860	71	6,128	6,049	79	2,808	2,775	33
Asthma incidence rate		1.8%			1.8%			1.3%			1.2%	
Age, years (Mean ± SD)	47.1±4.9	47.1±4.9	47.3±5.1	60.0±0	60.0±0	60.0±0	57.8±10.6	57.8±10.6	58.2±9.7	72.9±10.4	72.9±10.4	71.1±7.6
Age categories, N (%)												
< 65 years old	7,520 (100)	7,387 (100)	133 (100)	3,931 (100)	3,860 (100)	71 (100)	4,621 (75)	4,567 (76)	54 (68)	679 (24)	676 (24)	3 (9)
≥ 65 years old	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1,507 (25)	1,482 (24)	25 (32)	2,129 (76)	2,099 (76)	30 (91)
Female, N (%)	4,590 (61)	4,493 (61)	97 (73)	2,049 (52)	2,007 (52)	42 (59)	3,391 (55)	3,339 (55)	52 (66)	1,752 (62)	1,734 (62)	18 (55)

BMI, kg/m^2 (Mean ± SD)	25.7±4.0	25.7±4.0	26.6±4.4	26.8±4.2	26.8±4.2	27.8±5.3	24.6±3.4	24.5±3.4	25.7±3.4	25.6±4.3	25.6±4.3	25.8±4.2
BMI, WHO categories, N (%)												
<18.5	51 (1)	51 (1)	0 (0)	26 (1)	26 (1)	0 (0)	94 (2)	93 (2)	1 (1)	77 (3)	77 (3)	0 (0)
18.5–24.9	3,596 (48)	3,544 (48)	52 (39)	1,392 (35)	1,368 (35)	24 (34)	3,597 (59)	3,564 (59)	33 (42)	1,243 (44)	1,228 (44)	15 (45)
25.0–29.9	2,927 (39)	2,874 (39)	53 (40)	1,752 (45)	1,723 (45)	29 (41)	2,036 (33)	1,999 (33)	37 (47)	1,126 (40)	1,113 (40)	13 (39)
≥30.0	946 (13)	918 (12)	28 (21)	761 (19)	743 (19)	18 (25)	401 (7)	393 (6)	8 (10)	362 (13)	357 (13)	5 (15)
Smoking status, N (%)												
Current smoker	1,982 (26)	1,947 (26)	35 (26)	833 (21)	824 (21)	9 (13)	1,303 (36)	1,295 (21)	8 (10)	402 (14)	397 (14)	5 (15)
Previous smoker	2,737 (36)	2,682 (36)	55 (41)	1,514 (39)	1,484 (38)	30 (42)	2,039 (33)	2,011 (33)	28 (35)	1,072 (38)	1,058 (38)	14 (42)
Never smoker	2,801 (37)	2,758 (37)	43 (32)	1,584 (40)	1,552 (40)	32 (45)	2,786 (45)	2,743 (45)	43 (54)	1,334 (48)	1,320 (48)	14 (42)
Smoking duration, years (Mean ± SD)	12.7±13.0	12.7±13.0	13.6±13.3	15.5±16.3	15.5±16.3	15.3±16.3	14.7±17.0	14.8±17.0	10.3±14.1	15.6±19.2	15.6±19.2	18.1±20.4

Smoking intensity, n/day (Mean ± SD)	8.5±8.8	8.5±8.8	8.7±8.5	8.0±9.2	8.0±9.2	8.1±9.3	7.6±9.9	7.6±9.9	7.7±12.1	4.0 ±6.1	3.9±6.1	4.8±6.3
Marital status, N (%)												
Single	1,234 (16)	1,209 (16)	25 (19)	181 (5)	175 (5)	6 (8)	855 (14)	837 (14)	18 (23)	455 (16)	447 (16)	8 (24)
Married or living with partner	6,286 (84)	6,178 (84)	108 (81)	2,907 (74)	2,866 (74)	41 (58)	4,150 (68)	4,107 (68)	43 (54)	1,290 (46)	1,273 (46)	17 (52)
Divorced/Separated	0 (0)	0 (0)	0 (0)	642 (16)	624 (16)	18 (25)	688 (11)	676 (11)	12 (15)	386 (14)	383 (14)	3 (9)
Widowed	0 (0)	0 (0)	0 (0)	201 (5)	195 (5)	6 (8)	435 (7)	429 (7)	6 (8)	677 (24)	672 (24)	5 (15)
Employment status, N (%)												
Employed	6,826 (91)	6,705 (91)	121 (91)	2,669 (68)	2,623 (68)	46 (65)	3,948 (64)	3,905 (65)	43 (54)	651 (23)	647 (23)	4 (12)
Others	694 (9)	682 (9)	12 (9)	1,262 (32)	1,237 (32)	25 (35)	2,180 (36)	2,144 (35)	36 (46)	2,157 (77)	2,128 (77)	29 (88)
Educational levels, N (%)*												
Low level	2,370 (32)	2,338 (32)	32 (24)	1,570 (40)	1,547 (40)	23 (32)	1,635 (27)	1,615 (27)	20 (25)	708 (25)	701 (25)	7 (21)
Medium level	2,889 (38)	2,834 (38)	55 (41)	1,267 (32)	1,234 (32)	24 (34)	2,230 (36)	2,198 (36)	32 (41)	1,124 (40)	1,112 (40)	12 (36)

High level	2,261 (30)	2,215 (30)	46 (35)	1,094 (28)	1,070 (28)	24 (34)	2,263 (37)	2,236 (37)	27 (34)	976 (35)	962 (35)	14 (42)
COPD, N (%)#	0 (0)	0 (0)	0 (0)	4 (0.1)	4 (0.1)	0 (0)	17 (0.3)	16 (0.3)	1 (1)	25 (1)	24 (1)	1 (3)
Area-level mean year incomeϕ	24,340.7	24340.6	24341.9	24762.8	24769.3	24410.6	25305.5	25315.1	24576.2	28665.6	28665.6	28664.0

BMI, body mass index; SD, standard deviation; WHO, world health organization; COPD, chronic obstructive pulmonary disease.

*: Low educational level means primary school or less; Medium educational level means up to secondary school or equivalent; High educational level means university degree and more.

#: the prevalence of COPD among participants at baseline.

ϕ: Area-level mean year income is a continuous variable in euros, which is at municipality-level in 2001 for DCH and DNC and at neighbourhood level in 1994 for CEANS.

Table S3. Description of air pollutants by sub-cohorts and adult-onset asthma status for the year 2010.

Pollutants	Cohorts	Number of observations	Total			No Asthma			Asthma		
			Mean ± SD	Range	IQR	Mean ± SD	Range	IQR	Mean ± SD	Range	IQR
$PM_{2.5}$, µg/m^3											
	All	98,326	12.12±2.48	3.24–19.49	2.48	12.11±2.48	3.24–19.49	2.50	12.43±2.35	3.75–18.30	2.07
CEANS	SDPP	7,520	7.63±0.92	3.79–10.96	0.75	7.63±0.92	3.79–10.96	0.75	7.70±0.90	4.30–10.70	0.68
	SIXTY	3,931	8.31±0.92	3.24–11.01	0.88	8.30±0.92	3.24–11.01	0.89	8.63±0.56	7.12–10.11	0.59
	SALT	6,128	8.38±0.84	3.47–11.37	0.88	8.38±0.84	3.47–11.37	0.88	8.31±0.93	3.75–9.96	0.98
	SNAC-K	2,808	8.56±0.83	5.16–11.37	0.59	8.56±0.83	5.16–11.37	0.59	8.54±1.00	5.53–9.89	0.53
DCH	DCH	52,961	13.20±1.43	7.29–19.49	1.58	13.20±1.43	7.29–19.49	1.58	13.29±1.43	7.70–18.30	1.85
DNC	1993	16,937	12.74±1.54	6.48–19.14	1.87	12.74±1.54	6.48–19.14	1.86	12.91±1.54	9.55–16.93	1.93
	1999	8,041	13.80±1.51	6.89–19.49	2.34	13.80±1.51	6.89–19.49	2.34	13.66±1.61	9.58–16.81	2.54
NO_2, µg/m^3											
	All	98,326	25.10±7.97	2.68–72.23	11.88	25.08±7.97	2.68–72.23	11.88	26.25±7.79	5.68–62.36	11.80
CEANS	SDPP	7,520	15.47±4.29	2.96–37.09	5.39	15.47±4.29	2.96–37.09	5.38	15.78±4.46	6.24–26.10	5.85
	SIXTY	3,931	20.67±6.14	2.68–47.88	7.01	20.62±6.15	2.68–47.88	7.04	22.98±5.24	10.36–38.20	6.03

	SALT	6,128	21.29±6.18	2.98–50.32	7.34	21.29±6.19	2.98–50.23	7.33	21.30±5.79	5.68–39.79	7.39
	SNAC-K	2,808	27.41±5.08	11.62–42.61	7.31	27.40±5.08	11.62–42.61	7.38	27.79±7.86	16.44–35.02	6.19
DCH	DCH	52,961	28.03±6.83	6.40–72.23	9.98	28.01±6.84	6.40–72.23	10.00	28.96±6.42	9.50–62.36	9.32
DNC	1993	16,937	21.89±8.00	4.54–72.23	10.51	21.87±8.00	4.54–72.23	10.53	22.74±7.94	6.75–51.92	10.51
	1999	8,041	25.83±8.47	6.42–54.26	13.77	25.81±8.46	6.42–54.26	13.74	26.79±8.96	8.59–47.52	15.58
BC, $10^{-5}m^{-1}$											
	All	98,326	1.17±0.41	0.11–3.66	0.64	1.17±0.41	0.11–3.66	0.64	1.23±0.41	0.22–3.18	0.62
	SDPP	7,520	0.56±0.19	0.14–1.39	0.30	0.56±0.19	0.14–1.39	0.30	0.58±0.21	0.22–1.15	0.33
CEANS	SIXTY	3,931	0.80±0.25	0.11–2.10	0.32	0.80±0.25	0.11–2.10	0.32	0.90±0.25	0.28–1.50	0.31
	SALT	6,128	0.83±0.25	0.16–2.43	0.31	0.83±0.25	0.16–2.43	0.31	0.82±0.25	0.29–2.07	0.31
	SNAC-K	2,808	1.08±0.15	0.43–1.74	0.15	1.08±0.15	0.43–1.74	0.15	1.09±0.13	0.86–1.44	0.11
DCH	DCH	52,961	1.34±0.35	0.35–3.66	0.48	1.34±0.35	0.35–3.66	0.48	1.38±0.33	0.49–3.18	0.47
DNC	1993	16,937	1.09±0.37	0.13–3.66	0.52	1.09±0.37	0.13–3.66	1.52	1.12±0.37	0.34–2.49	0.52
	1999	8,041	1.30±0.38	0.36–2.74	0.55	1.29±0.38	0.36–2.74	0.55	1.35±0.40	0.56–2.30	0.74
O_3, μg/m^3											
	All	98,326	78.12±4.62	50.96–91.87	6.00	78.13±4.61	50.96–91.87	6.00	77.95±4.81	59.58–90.24	6.09

	SDPP	7,520	77.55±1.92	68.37–85.01	2.59	77.55±1.92	68.37–85.01	2.59	77.59±1.98	71.55–82.10	2.81
CEANS	SIXTY	3,931	76.70±2.52	63.15–83.79	2.88	76.72±2.52	63.15–83.79	2.90	75.82±2.50	68.60–81.28	2.96
	SALT	6,128	76.57±2.73	57.17–84.87	2.87	76.56±2.73	57.17–84.87	2.88	76.80±2.42	64.54–82.58	2.27
	SNAC-K	2,808	75.11±2.65	58.63–82.50	2.91	75.11±2.66	58.63–82.50	2.91	74.87±2.11	69.21–77.96	2.58
DCH	DCH	52,961	77.54±5.10	50.96–87.79	7.15	77.54±5.10	50.96–87.79	7.15	77.38±5.17	59.58–86.96	7.37
DNC	1993	16,937	80.41±4.00	50.96–91.87	3.95	80.42±3.99	50.96–91.87	3.95	79.99±4.57	61.37–90.06	4.25
	1999	8,041	80.62±3.83	57.02–91.83	3.88	80.63±3.83	57.02–91.83	3.87	80.19±4.16	61.85–90.24	4.34

$PM_{2.5}$, particulate matter with diameter < 2.5 μm; NO_2, nitrogen dioxide; BC, black carbon; O_3, ozone.

The annual average concentrations of $PM_{2.5}$, NO_2, BC and O_3 were estimated for the year 2010 at 100 m resolution. O_3 was estimated during the warm season from April 1 through September 30.

Table S4. Characteristics of participants at baseline (1992–2004) and air pollutants for the year 2010 by the quintiles of NO_2 concentrations.

Characteristic	NO_2 quintiles				
	1st	2nd	3rd	4th	5th
NO_2, µg/m^3 (Range)	2.68–17.87	17.87–22.51	22.51–27.31	27.31–32.59	32.59–72.23
No of participants, N	19,665	19,664	19,666	19,665	19,666
Age, years (Mean ± SD)	53.43 ± 7.85	55.52 ± 7.83	56.52 ± 7.35	57.57 ± 7.28	55.89 ± 6.50
Female, N (%)	13,762 (70)	13,528 (69)	12,641 (64)	11,866 (60)	12,695 (65)
BMI, kg/m^2 (Mean ± SD)	25.10 ± 3.92	25.04 ± 3.86	25.34 ± 4.00	25.74 ± 4.16	25.47 ± 4.17
Normal weight, N (%)*	10,487 (53)	10,507 (53)	10,015 (51)	9,113 (46)	9,779 (50)
Smoking duration	14.80 ± 15.31	15.87 ± 16.12	17.13 ± 16.77	18.09 ± 17.16	19.58 ± 16.77
Smoking intensity	8.50 ± 9.87	8.61 ± 9.96	9.11 ± 10.44	9.44 ± 10.68	10.50 ± 10.76
Never smoker, N (%)	7,607 (39)	7,670 (39)	7,497 (38)	7,346 (37)	6,275 (32)
Married or living with partner, N (%)	16,050 (82)	15,032 (76)	14,042 (71)	13,278 (68)	11,743 (60)
Employed, N (%)	15,573 (79)	14,840 (75)	14,593 (74)	14,351 (73)	15,754 (80)
High educational level, N (%)	10,578 (54)	9,791 (50)	8,160 (41)	6,684 (34)	8,097 (41)
Mean year income, €ϕ	21154.41	20985.80	21083.05	21213.40	20522.29

$PM_{2.5}$, µg/m^3 (Mean ± SD)	9.93 ± 2.38	11.16 ± 2.09	12.16 ± 1.81	13.00 ± 1.74	14.33 ± 1.74
BC, $10^{-5}m^{-1}$ (Mean ± SD)	0.66 ± 0.19	0.94 ± 0.19	1.16 ± 0.16	1.41 ± 0.21	1.70 ± 0.22
O_3, µg/m^3 (Mean ± SD)	80.43 ± 2.71	79.35 ± 2.97	78.80 ± 4.07	78.43 ± 3.70	73.60 ± 5.67

*: Normal weight means BMI values from 18.5 to 24.9 according to the World Health Organization (WHO) categories; High educational level means university degree and more.

ϕ: Mean year income is a continuous variable in euros, which is at municipality level in 2001 for DCH and DNC and at neighbourhood level in 1994 for CEANS.

Figure S1. The temporal variations of annual mean air pollution concentrations back-extrapolated using the ratio (left) and the absolute difference (right) method during follow-up periods (1992-2011 for CEANS and 1993-2015 for DCH) in 71,311 participants of CEANS (N=19,320) and DCH (N=51,991) cohorts**.**

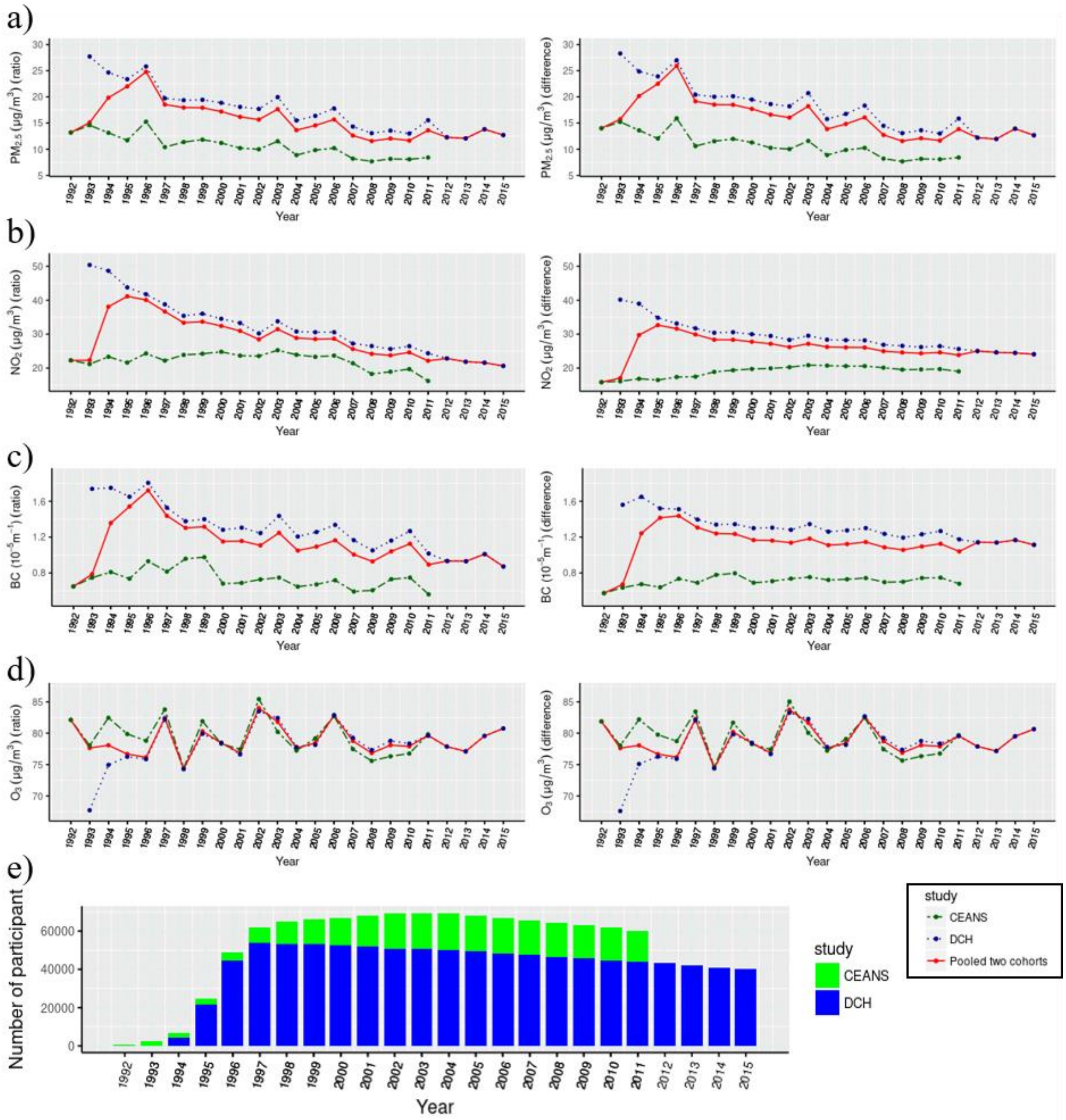


Table S5. Pearson correlations between air pollutants by sub-cohorts for the year 2010.

Cohorts	Number of observations	Pollutants	$PM_{2.5}$	NO_2	BC	O_3
All	98,326					
		$PM_{2.5}$	1.00			
		NO_2	0.63	1.00		
		BC	0.74	0.91	1.00	
		O_3	-0.13	-0.48	-0.37	1.00
CEANS- SDPP	7,520					
		$PM_{2.5}$	1.00			
		NO_2	0.60	1.00		
		BC	0.49	0.67	1.00	
		O_3	-0.18	-0.70	-0.33	1.00
CEANS- SIXTY	3,931					
		$PM_{2.5}$	1.00			
		NO_2	0.69	1.00		
		BC	0.59	0.84	1.00	
		O_3	-0.45	-0.71	-0.71	1.00
CEANS- SALT	6,128					
		$PM_{2.5}$	1.00			
		NO_2	0.67	1.00		
		BC	0.55	0.84	1.00	
		O_3	-0.47	-0.74	-0.76	1.00
CEANS- SNAC-K	2,808					
		$PM_{2.5}$	1.00			
		NO_2	0.75	1.00		
		BC	0.28	0.43	1.00	

		O_3	-0.49	-0.65	-0.74	1.00
DCH	52,961					
		$PM_{2.5}$	1.00			
		NO_2	0.72	1.00		
		BC	0.66	0.91	1.00	
		O_3	-0.56	-0.61	-0.57	1.00
DNC-1993	16,937					
		$PM_{2.5}$	1.00			
		NO_2	0.64	1.00		
		BC	0.69	0.92	1.00	
		O_3	-0.32	-0.42	-0.42	1.00
DNC-1999	8,041					
		$PM_{2.5}$	1.00			
		NO_2	0.61	1.00		
		BC	0.64	0.93	1.00	
		O_3	-0.16	-0.21	-0.20	1.00

Table S6. Results for threshold analyses of associations between long-term air pollution exposure and adult-onset asthma based on Model 3 (N=98,326).

Pollutants	Threshold	AIC	HR (95%CI)
$PM_{2.5}$	No threshold	36807.6	1.22 (1.04–1.43)
	5 μg/m^3	36807.61	1.22 (1.04–1.43)
	7.5 μg/m^3	36807.78	1.22 (1.04–1.43)
	10 μg/m^3	36808.71	1.20 (1.02–1.42)
NO_2	No threshold	36790.44	1.17 (1.10–1.25)
	10 μg/m^3	36790.73	1.17 (1.10–1.25)
	15 μg/m^3	36791.04	1.18 (1.10–1.26)
	20 μg/m^3	36796.19	1.17 (1.09–1.26)
BC	No threshold	36795.5	1.15 (1.08–1.23)
	0.5 $10^{-5}m^{-1}$	36795.68	1.15 (1.08–1.23)
	1 $10^{-5}m^{-1}$	36801.14	1.15(1.07–1.25)
	1.5 $10^{-5}m^{-1}$	36810.49	1.16 (0.98–1.37)
O_3	No threshold	36809.26	0.90 (0.81–0.99)
	40 μg/m^3	36809.26	0.90 (0.81–0.99)
	60 μg/m^3	36809.22	0.90 (0.81–0.99)
	80 μg/m^3	36811.37	0.78 (0.56–1.09)

AIC, Akaike Information Criterion. Results are presented as hazard ratio (HR) and 95% confidence interval (CI) [HR (95%CI)] for the following increases: 5 μg/m^3 for $PM_{2.5}$, 10 μg/m^3 for NO_2, 0.5 10^{-5} m^{-1} for BC and 10 μg/m^3 for O_3.

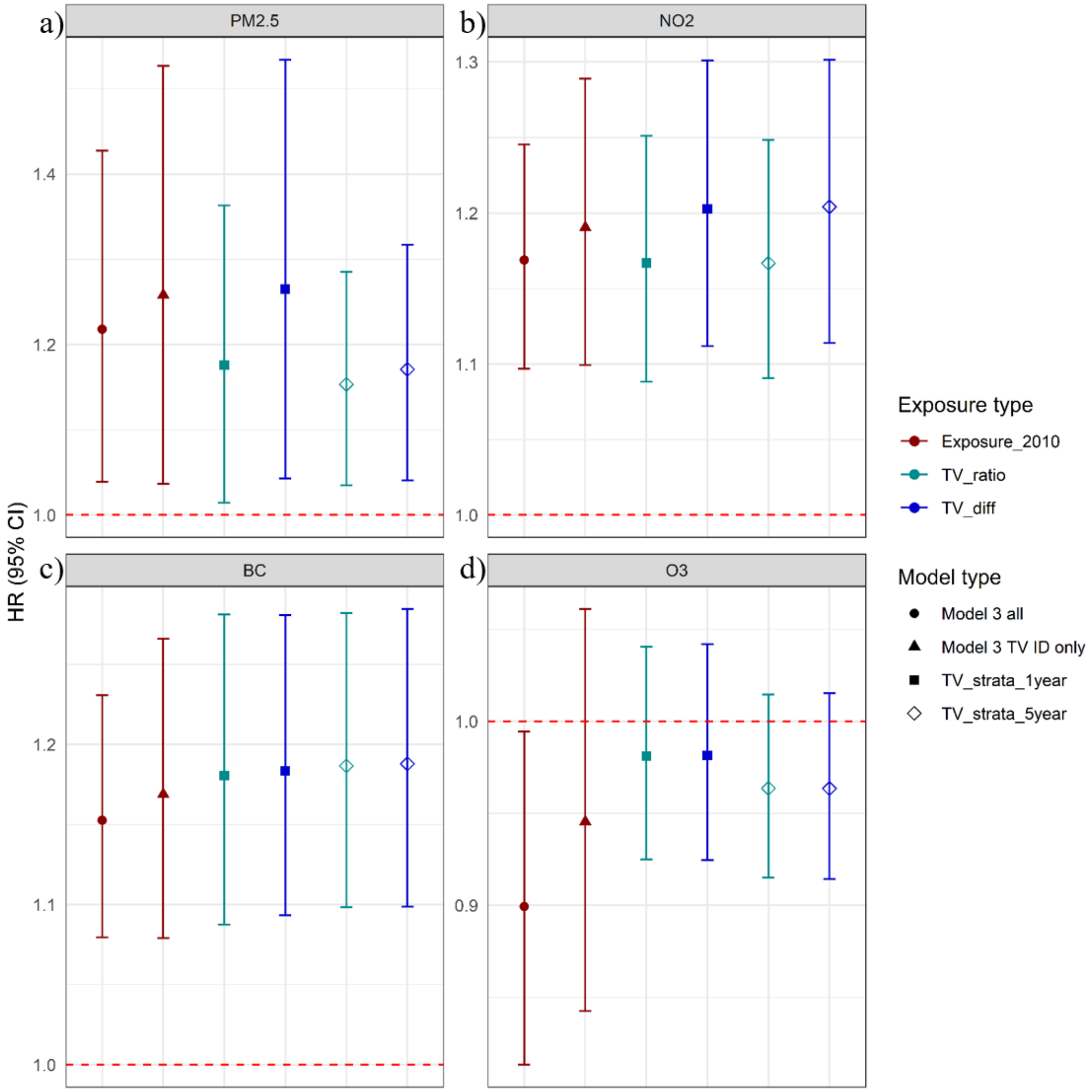
*: Lower AIC values represent improved prediction of models for the associations.

Table S7. Results for Sensitivity Analysis by time-varying exposure analyses among two cohorts with available information (CEANS and DCH, N=71,311) based on Model 3.

Pollutants	**Main model 3**	**Time-varying analyses**			
	Reduced dataset (N=71,311)	Strata by per year of follow-up time		Strata by 5-years of follow-up time	
		Ratio method	Difference method	Ratio method	Difference method
$PM_{2.5}$	1.26 (1.04–1.53)	1.18 (1.01–1.36)	1.26 (1.04–1.53)	1.15 (1.03–1.29)	1.17 (1.04–1.32)
NO_2	1.19 (1.10–1.29)	1.17 (1.09–1.25)	1.20 (1.11–1.30)	1.17 (1.09–1.25)	1.20 (1.11–1.30)
BC	1.17 (1.08–1.27)	1.18 (1.09–1.28)	1.19 (1.09–1.28)	1.19 (1.10–1.28)	1.19 (1.10–1.28)
O_3	0.95 (0.84–1.06)	0.98 (0.92–1.04)	0.98 (0.92–1.04)	0.96 (0.92–1.01)	0.96 (0.91–1.02)

Results are presented as hazard ratio and 95% confidence interval [HR (95%CI)] for the following increases: 5 $\mu g/m^3$ for $PM_{2.5}$, 10 $\mu g/m^3$ for NO_2, 0.5 10^{-5} m^{-1} for BC, and 10 $\mu g/m^3$ for O_3.

Figure S2. Results for Sensitivity Analysis by time-varying exposure analyses among two cohorts with available information (CEANS and DCH, N=71,311) based on Model 3.



Three different exposure types were applied: Exposure_2010 indicates exposure in 2010; TV_ratio indicates time-varying exposure analysis with a ratio method; TV_ratio indicates time-varying exposure analysis with an absolute difference method.

Four different exposure types were applied: Model 3 all indicates using model 3 with all cohort participants; Model 3 TV ID only indicates using model 3 with time-varying exposure analysis available two cohort participants; TV_strata_1year indicates time-varying exposure analysis with 1-year strata for the calendar time; TV_strata_5year indicates time-varying exposure analysis with 5-year strata for the calendar time.

Table S8. Back-extrapolated air pollution exposure at baseline and adult-onset asthma based on Model 3.

Pollutants	Main model 3	Baseline exposure analyses	
	(N=98,326)	Ratio method	Difference method
$PM_{2.5}$	1.22 (1.04–1.43)	1.04 (0.96–1.12)	0.98 (0.89–1.09)
NO_2	1.17 (1.10–1.25)	1.12 (1.07–1.17)	1.17 (1.10–1.25)
BC	1.15 (1.08–1.23)	1.11 (1.05–1.18)	1.15 (1.07–1.23)
O_3	0.90 (0.81–0.99)	0.95 (0.87–1.05)	0.95 (0.86–1.05)

Results are presented as hazard ratio and 95% confidence interval [HR (95%CI)] for the following increases: 5 $\mu g/m^3$ for $PM_{2.5}$, 10 $\mu g/m^3$ for NO_2, 0.5 10^{-5} m^{-1} for BC, and 10 $\mu g/m^3$ for O_3.

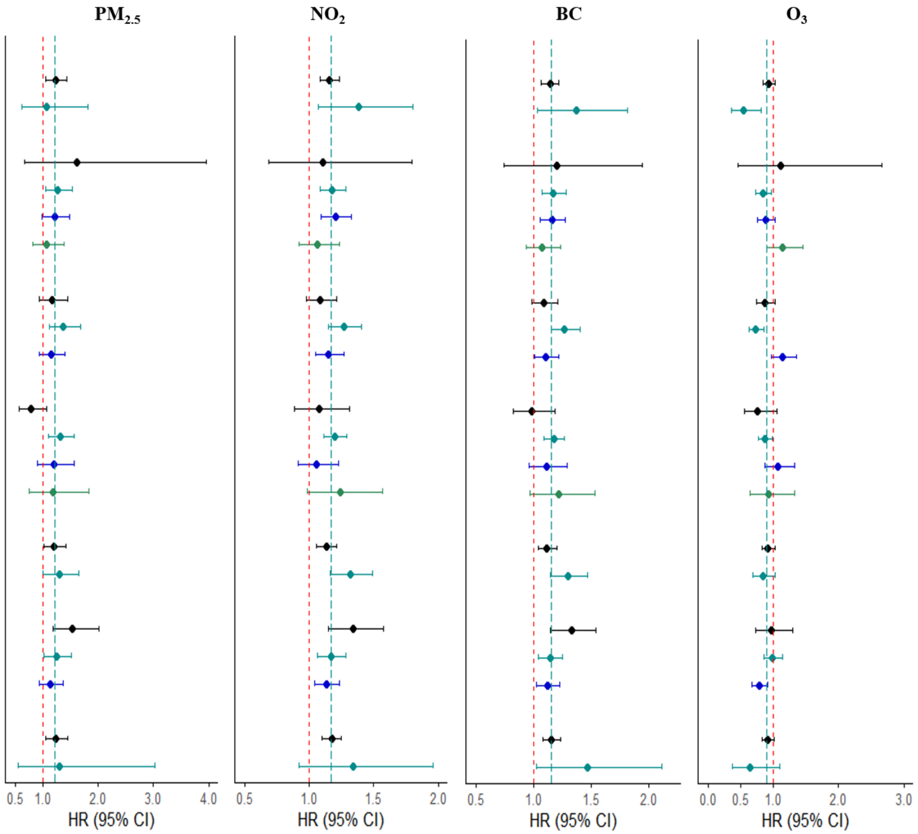
Table S9. Results for Sensitivity Analysis by restricting participants to different cohorts in Model 3.

Cohorts	**Number of observations**	**HR (95%CI)**			
		$PM_{2.5}$	**NO_2**	**BC**	**O_3**
All cohorts	98,326	1.22 (1.04–1.43)	1.17 (1.10–1.25)	1.15 (1.08–1.23)	0.90 (0.81–0.99)
Exclude CEANS	77,939	1.24 (1.06–1.47)	1.17 (1.10–1.26)	1.15 (1.08–1.23)	0.87 (0.79–0.97)
Exclude DCH	45,365	1.18 (0.91–1.53)	1.14 (1.04–1.25)	1.15 (1.03–1.28)	0.79 (0.65–0.95)
Exclude DNC	73,348	1.25 (1.03–1.51)	1.19 (1.10–1.29)	1.17 (1.08–1.26)	0.95 (0.84–1.06)
Only CEANS	20,387	1.42 (0.74–2.71)	1.15 (0.93–1.41)	1.24 (0.97–1.59)	0.88 (0.55–1.39)
Only DCH	52,961	1.26 (1.02–1.57)	1.21 (1.10–1.33)	1.16 (1.06–1.27)	0.93 (0.82–1.06)
Only DNC	24,978	1.17 (0.88–1.56)	1.14 (1.02–1.27)	1.13 (1.01–1.28)	0.74 (0.60–0.92)

Results are presented as hazard ratio and 95% confidence interval [HR (95%CI)] for the following increases: 5 $\mu g/m^3$ for $PM_{2.5}$, 10 $\mu g/m^3$ for NO_2, 0.5 10^{-5} m^{-1} for BC and 10 $\mu g/m^3$ for O_3.

Figure S3. Effect modification on the association of long-term air pollution exposure with adult-onset asthma by baseline characters.

Baseline characters	Numbers	P valueϕ
Age, years		
<65	91,318	$PM_{2.5}$: 0.59; NO_2: 0.19
≥65	7,008	BC: 0.22; O_3: 0.01*
BMI, kg/m²		
<18.5	1,298	
18.5-24.9	49,901	$PM_{2.5}$: 0.55; NO_2: 0.54
25.0-29.9	35,604	BC: 0.71; O_3: 0.16
≥30.0	11,523	
Smoking status		
Current smoker	32,398	
Previous smoker	29,533	$PM_{2.5}$: 0.25; NO_2: 0.09
Never smoker	36,395	BC: 0.04*; O_3: <0.01*
Marital status		
Single	8,450	
Married or with partner	70,137	$PM_{2.5}$: 0.01*; NO_2: 0.33
Divorced/Separated	13,755	BC: 0.30O_3: 0.22
Widowed	5,984	
Employment status		
Employed	75,111	$PM_{2.5}$: 0.56; NO_2: 0.03*
Others	23,215	BC: 0.03*; O_3: 0.42
Educational levels#		
Low level	14,102	
Medium level	40,914	$PM_{2.5}$: 0.08; NO_2: 0.16
High level	43,310	BC: 0.10; O_3: 0.08
COPD		
Non-COPD participant	97,841	$PM_{2.5}$: 0.92; NO_2: 0.49
COPD patient	485	BC: 0.20; O_3: 0.20



Effect modification analyses were conducted based on Model 3 and evaluated by introducing interaction terms. *P* values for whether there were statistical differences between strata were tested by the Wald test. Red long dash lines indicate the HRs equal to 1 and green long dash lines indicate the estimated HRs for all participants based on Model 3.

#: Low educational level means primary school or less; Medium educational level means up to secondary school or equivalent; High educational level means university degree and more.

*: A statistically significant *P* value (at 5% level) for effect modification analyses.