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}, NO₂, BC, and warm season O₃ (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}, NO₂, and O₃ 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%), NO₂ (59%), BC (54%), and O₃ (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 (NO2 and O₃) and 2013 model for PM_{2.5} at the overall European scale, with squared correlations (R²) 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.,			Salf reported authma diagnosad		RR (95% CI):
,	The Ahsmog Study, California, USA,	3,091 non-smokers	Self-reported asthma diagnosed	O ₃ (46.5 ppb)	M: 2.09 (1.03–4.16) per 27 ppb
1999 [12]			by a doctor		F: 0.86 (0.58–1.26) per 27 ppb
Jacquemin et al.,	European Respiratory Health Survey	1 105	Self-reported ever asthma	NO ₂ (median: 27.7	OR (95% CI):
2009 [13]	(ECRHS), 17 European cities	4,185	diagnosed by a doctor	$\mu g/m^3$)	1.43 (1.02–2.01) per 10 μ g/m ³
Künzli et al.,	TI CARALDIA I GC 's I I	2.725	Self-reported doctor-diagnosed	ITTD14 (0.50 / 3)	HR (95% CI):
2009 [14]	The SAPALDIA cohort, Switzerland	2,725 never-smokers	asthma	$dTPM_{10}$ (-0.59 µg/m ³)	1.30 (1.05–1.61) per 1 μ g/m ³
Modig et al.,	The Respiratory Health in Northern	2.600	Self-reported asthma with	NO (17.0 / 3)	OR (95% CI):
2009 [15]	Europe (RHINE) cohort, Sweden	3,609	questionnaire	$NO_2 (17.9 \mu g/m^3)$	$1.54 (1.00-2.36) \text{ per } 10 \mu\text{g/m}^3$
			Hospital contact (in-, outpatient,		HR (95% CI):
Andersen et al.,	The Diet, Cancer and Health cohort,	57,053	or emergency) primary discharge	NO ₂ (median: 15.2 μg/m ³)	1.10 (1.01–1.20) per 5.8 μ g/m ³
2012 [16]	Denmark		diagnoses ICD-10: J45-46		
Young et al.,	The Gioten Cander LICA	50,884 women	Self-reported doctor diagnosed	NO ₂ (median: 9.3 ppb)	OR (95% CI):
2014 [17]	The Sister Study, USA	(sisters with breast	asthma	PM _{2.5} (median 10.8	1.12 (0.96–1.30) per 5.8 ppb

		cancer)		μg/m³)	1.20 (0.99–1.46) per 3.6 μ g/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/m³ by cohort) PM _{2.5} (mean range 10–18 μg/m³ by cohort) PM _{2.5absorbance} (mean range 1.0–2.1 10 ⁻⁵ m ⁻¹ by	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	cohort) 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 claims, hospital admissions and medication data): ICD-9: 493	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 1.00 (1.00–1.01) per 10,097 count/cm ³

					HR (95% CI):
Salimi et al.,	The Sax Institute's 45 and Up Study,		Primary diagnosis of	$NO_2 (17.5 \mu g/m^3)$	
		100,084			$1.03 (0.88-1.19) \text{ per 5 } \mu\text{g/m}^3$
2018 [21]	Sydney, Australia		hospitalization ICD-10: J45-46	$PM_{2.5} (4.5 \mu g/m^3)$	
					$1.08 (0.89-1.30) \text{ per } 1 \mu\text{g/m}^3$

 $PM_{2.5}$, particulate matter with diameter < $2.5 \mu m$; dTPM₁₀, the difference in traffic-related particulate matter with diameter < $10 \mu m$; NO₂, nitrogen dioxide; BC, black carbon; O₃, 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 NO₂: 1 ppb = $1.88 \ \mu g/m^3$; for O₃: 1 ppb = $2.00 \ \mu g/m^3$.

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

	All o	ohorts (N=98	326)	D	CH (N=52,96	(1)			DNC (N	=24,978)		
Characteristic at baseline*	All C	onorts (14–20,	,320)		CH (11–32,90) 1)	19	93 (N=16,93	37)	19	999 (N=8,04	1)
Characteristic at basenine	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 $(Mean \pm SD)$	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	89,462	1,856	52,335	51,203	1,132 (99)	14,318	14,002	316 (90)	7,914	7,767	147 (99)
< 03 years old	(93)	(93)	(94)	(99)	(99)	1,132 (99)	(85)	(84)	310 (90)	(98)	(98)	147 (33)
≥ 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	63,073	1,419	27,732	27,023	709 (62)	16,937	16,585	352	8,041	7,892	149
remaie, iv (70)	(66)	(65)	(72)	(52)	(52)	709 (02)	(100)	(100)	(100)	(100)	(100)	(100)
BMI, kg/m^2 (Mean \pm 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)
19.5. 24.0	49,901	49,007	904 (45)	22,893	22,436	457 (40)	11,688	11,467	221 (62)	5,492	5,400	02 (62)
18.5–24.9	(51)	(51)	894 (45)	(43)	(43)	457 (40)	(69)	(69)	221 (63)	(68)	(68)	92 (62)
25.0.20.0	35,604	34,867	727 (29)	22,013	21,536	477 (42)	3,875	3,790	95 (24)	1,875	1,832	42 (20)
25.0–29.9	(36)	(36)	737 (38)	(42)	(42)	477 (42)	(23)	(23)	85 (24)	(23)	(23)	43 (29)
≥30.0	11,523	11,214	200 (16)	7.620 (14)	7 427 (14)	202 (18)	970 (5)	944 (5)	25 (10)	525 (7)	522 (7)	12 (0)
≥30.0	(12)	(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 (%)												
Compart amalian	32,398	31,842	556 (29)	19,218	18,869	240 (20)	6,357	6,247	110 (21)	2,303	2,263	40 (27)
Current smoker	(33)	(33)	556 (28)	(36)	(36)	349 (30)	(38)	(38)	110 (31)	(29)	(29)	40 (27)
D : 1	29,533	28,884	640 (22)	14,728	14,371	257 (21)	4,824	4,711	112 (22)	2,619	2,567	50 (25)
Previous smoker	(30)	(30)	649 (33)	(28)	(28)	357 (31)	(28)	(28)	113 (32)	(33)	(33)	52 (35)
Never smoker	36,395	35,635	760 (39)	19,045	18,573	442 (39)	5,756	5,627	129 (37)	3,119	3,062	57 (38)

	(37)	(37)		(36)	(36)		(34)	(34)		(39)	(39)	
Smoking duration, years $(Mean \pm SD)$	17.1±16.5	17.1±16.5	16.1±16.	19.1±17.2	19.1±17.2	17.7±16.7	16.5±15.	16.5±15.	14.6±15.	12.5±12.	12.5±12.	12.8±12.
Smoking intensity, n/day (Mean \pm 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	70,137	68,790	1,347	37,928	37,130	798 (70)	11,471	11,235	236 (67)	6,105	6,001	104 (70)
partner	(71)	(71)	(69)	(72)	(72)	198 (10)	(68)	(68)	230 (07)	(76)	(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	73,616	1,495	41,519	40,650	960 (76)	11,877	11,609	269 (76)	7,621	7,477	144 (07)
Employed	(76)	(76)	(76)	(78)	(78)	869 (76)	(70)	(70)	268 (76)	(95)	(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	13,845	257 (13)	7,819 (15)	7,644 (15)	175 (15)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Low level	(14)	(14)	237 (13)	7,015 (13)	7,011 (13)	175 (15)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
M. P	40,914	40,031	002 (45)	33,404	32,644	7(0)((()	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Medium level	(42)	(42)	883 (45)	(63)	(63)	760 (66)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
TT 1 1 1	43,310	42,485	025 (12)	11,738	11,525	212 (10)	16,937	16,585	352	8,041	7,892	149
High level	(44)	(44)	825 (42)	(22)	(22)	213 (19)	(100)	(100)	(100)	(100)	(100)	(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												
income¢	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.

	CEANS (N=20,387)										
Characteristic at baseline*	SDPP (N=7,	520)	SIXTY (N=	3,931)	SALT (I	N=6,128)	SNAC-K (N=2,808)				
_	No		No		N	lo	No				
	Total	Asthma	Total	Asthma	Total	Asthma	Total Asthma				
	asthma	1	asthma	1	astl	hma	asth	ma			
Enrollment period	1992–199	98	1997–19	99	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.	57.8±10.	58.2±9.7	72.9±10.	72.9±10.	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 \pm 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	3,564	33 (42)	1,243	1,228	15 (45)
10.5 21.5	2,270 (10)	3,3 11 (10)	32 (37)	1,592 (55)	1,500 (55)	2. (3.)	(59)	(59)	33 (12)	(44)	(44)	13 (13)
25.0–29.9	2,927 (39)	2,874 (39)	53 (40)	1,752 (45)	1,723 (45)	29 (41)	2,036	1,999	37 (47)	1,126	1,113	13 (39)
23.0 25.5	2,527 (35)	2,071 (37)	33 (10)	1,732 (13)	1,723 (13)	25 (11)	(33)	(33)	37 (17)	(40)	(40)	13 (37)
≥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	1,295	8 (10)	402 (14)	397 (14)	5 (15)
Current smoker	1,702 (20)	1,547 (20)	33 (20)	033 (21)	024 (21)) (13)	(36)	(21)	0 (10)	402 (14)	377 (14)	3 (13)
Previous smoker	2,737 (36)	2,682 (36)	55 (41)	1,514 (39)	1,484 (38)	30 (42)	2,039	2,011	28 (35)	1,072	1,058	14 (42)
i ie vious smokei	2,737 (30)	2,002 (30)	33 (41)	1,314 (37)	1,404 (30)	30 (42)	(33)	(33)	20 (33)	(38)	(38)	14 (42)
Never smoker	2,801 (37)	2,758 (37)	43 (32)	1,584 (40)	1,552 (40)	32 (45)	2,786	2,743	43 (54)	1,334	1,320	14 (42)
Never shorer	2,001 (37)	2,738 (37)	43 (32)	1,364 (40)	1,332 (40)	32 (43)	(45)	(45)	43 (34)	(48)	(48)	14 (42)
Smoking duration, years	12.7±13.0	12.7±13.0	13.6±13.	15.5±16.3	15.5±16.3	15.3±16.3	14.7±17.	14.8±17.	10.3±14.	15.6±19.	15.6±19.	18.1±20.
$(Mean \pm SD)$	12.7±13.0	12.7±13.0	3	13.3±10.3	13.3±10.3	13.3±10.3	0	0	1	2	2	4
Smoking intensity, n/day	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
$(Mean \pm SD)$	0.J±0.ŏ	0.3±0.6	0./±0.3	8.U±9.2	6.0±9.∠	0.1±9.3	7.0±9.9	7.0±9.9	/./±1 <i>2</i> .1	4.0 ±0.1	3.9±0.1	4.0±0.3
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	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												
:	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
incomeφ												

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		Total		N	o Asthma		Asthma		
1 onutants			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
	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
CEANS	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
	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
CEANS	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	1										
	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
	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

PM_{2.5}, particulate matter with diameter < 2.5 μm; NO₂, nitrogen dioxide; BC, black carbon; O₃, 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 NO₂ concentrations.

Characteristic	NO ₂ quintiles							
Characteristic	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 \pm 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 \pm 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			

$PM_{2.5}$, $\mu g/m^3$ (Mean \pm 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 , $\mu g/m^3$ (Mean \pm 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.

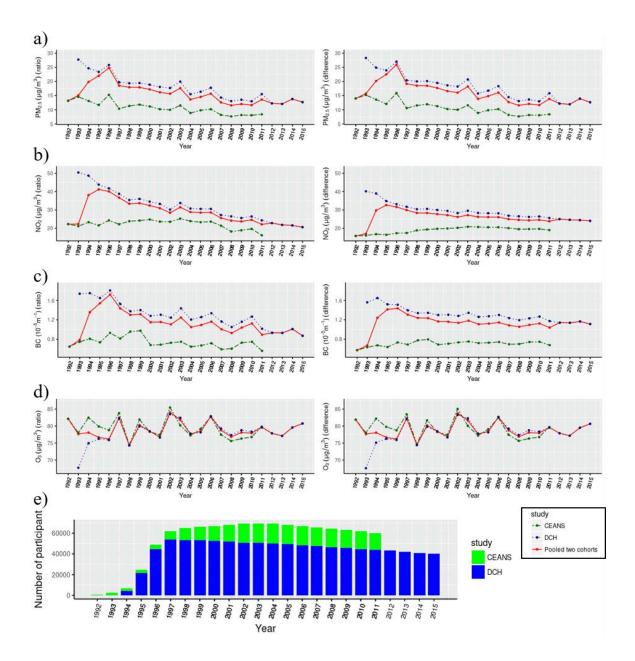


Table S5. Pearson correlations between air pollutants by sub-cohorts for the year 2010.

Cohorts	Number of observations	Pollutants	PM _{2.5}	NO ₂	ВС	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		
		ВС	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		
		ВС	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					
DATE TO DETECT	2,000	PM _{2.5}	1.00			
		NO ₂	0.75	1.00		
					1.00	
		ВС	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)
	$5 \mu g/m^3$	36807.61	1.22 (1.04–1.43)
	$7.5 \mu g/m^3$	36807.78	1.22 (1.04–1.43)
	$10 \ \mu \text{g/m}^3$	36808.71	1.20 (1.02–1.42)
NO_2	No threshold	36790.44	1.17 (1.10–1.25)
	$10 \mu \text{g/m}^3$	36790.73	1.17 (1.10–1.25)
	$15 \mu g/m^3$	36791.04	1.18 (1.10–1.26)
	$20 \ \mu g/m^3$	36796.19	1.17 (1.09–1.26)
BC	No threshold	36795.5	1.15 (1.08–1.23)
	$0.5 \ 10^{-5} \text{m}^{-1}$	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)
	$40~\mu g/m^3$	36809.26	0.90 (0.81-0.99)
	$60 \mu \text{g/m}^3$	36809.22	0.90 (0.81-0.99)
	$80 \ \mu g/m^3$	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 μ g/m³ for PM_{2.5}, 10 μ g/m³ for NO₂, 0.5 10⁻⁵ m⁻¹ for BC and 10 μ g/m³ for O₃.

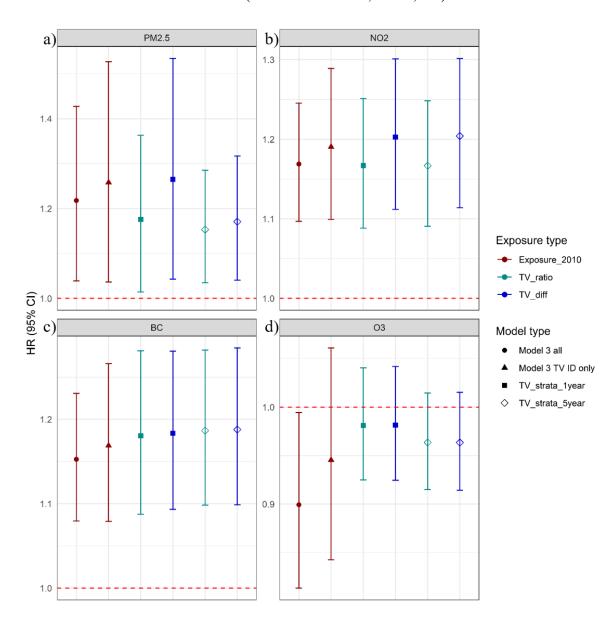
^{*:} Lower AIC values represent improved prediction of models for the associations.

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.

	Main model 3		Time-varying analyses						
Pollutants	Reduced dataset	Strata by per year	of follow-up time	Strata by 5-years of follow-up time					
	(N=71,311)	Difference		D (1 1	Difference				
	(11–71,311)	Ratio method	method	Ratio method	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 μ g/m³ for PM_{2.5}, 10 μ g/m³ for NO₂, 0.5 10⁻⁵ m⁻¹ for BC, and 10 μ g/m³ for O₃.

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.

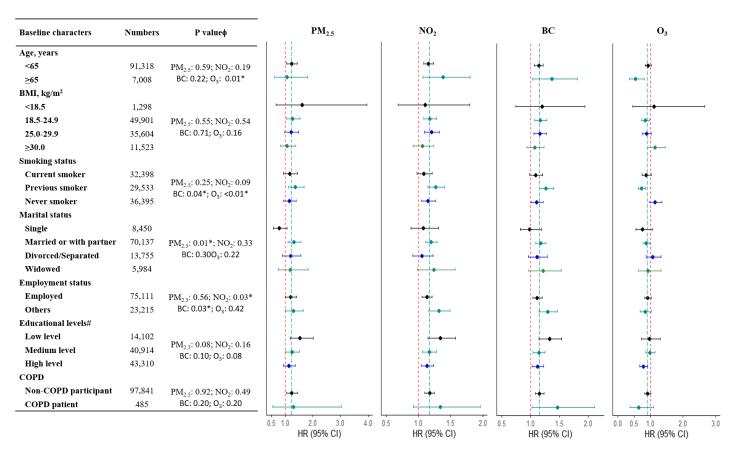
	Main model 3	Baseline exp	oosure analyses
Pollutants			
	(N=98,326)	Ratio method	Difference method
PM _{2.5}	1.22 (1.04–1.43)	1.04 (0.96–1.12)	0.98 (0.89–1.09)
NO_2	1.17 (1.10–1.25)	1.12 (1.07–1.17)	1.17 (1.10–1.25)
BC	1.15 (1.08–1.23)	1.11 (1.05–1.18)	1.15 (1.07–1.23)
O_3	0.90 (0.81-0.99)	0.95 (0.87–1.05)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

Results are presented as hazard ratio and 95% confidence interval [HR (95%CI)] for the following increases: 5 μ g/m³ for PM_{2.5}, 10 μ g/m³ for NO₂, 0.5 10⁻⁵ m⁻¹ for BC, and 10 μ g/m³ for O₃.

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

Calcarta	Number of		HR (95%CI)						
Cohorts	observations	$PM_{2.5}$	NO_2	ВС	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 a	as hazard ratio and 95% o	confidence interval [HR (9	5%CI)] for the followin	g increases: 5 μg/m³ for	PM _{2.5} , 10 μg/m ³ for				
NO_2 , 0.5	10^{-5} m ⁻¹	for BC	and 1	$\mu g/m^3$	for O_3 .				

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



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.