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Supplementary appendix

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Air pollution drives development of asthma, but not rhinoconjunctivitis through childhood and adolescence

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Supplementary Appendix

Materials and Methods

Study designs and study populations

For the BAMSE birth cohort study, between February 1994 and November 1996, 4089 new-born infants were recruited from Child Health Centres. The study population comprised 75% of all eligible children born in 4 predefined areas of central and north-western parts of Stockholm, representing urban and suburban environments.

For the GINIplus birth cohort study, a total of 5991 new-borns were recruited across the two German cities of Munich (2949 children) and Wesel (3042 children) from 1995 to 1998. Children with a family history of allergy (N=2252) had the opportunity to participate in a prospective, double-blinded nutritional intervention aimed at assessing the effect of different baby formulas on allergy development. Children without a family history of allergy (or those who declined to participate in the intervention) were assigned to the non-intervention group (N=3739).

For the LISAplus birth cohort study, neonates were recruited from four German cities of Munich (1467 children), Wesel (348 children), Leipzig (976 children) and Bad Honnef (306 children). Recruitment took place in obstetric clinics shortly after birth. From December 1997 to January 1999, the target population of the study was defined as new-borns from parents who were born in Germany and have German nationality. Neonates fulfilling at least one of the following criteria were excluded from the study: premature birth (maturity at <37 gestational weeks); low birth weight (<2500 g); congenital malformation; symptomatic intensive medical care during the neonatal period; immune-related diseases of the mother, such as autoimmune disorders; diabetes; hepatitis B; long-term medication use; or abuse of drugs or alcohol.

For the PIAMA birth cohort study, pregnant women were recruited in 1996-1997 during their second trimester of pregnancy from a series of communities in the North, West, and Centre of The Netherlands. Non-allergic pregnant women were invited to participate in a "natural history" study arm. Pregnant women identified as allergic through a validated screening questionnaire were primarily allocated to an intervention arm with a random subset allocated to the natural history arm. The intervention involved the use of mite-impermeable mattress and pillow covers.

Measurements of specific IgE

In the BAMSE cohort, all participants who returned questionnaires at ages 4, 8, and 16 years were invited for medical examinations including collection of blood samples. All blood samples were analysed for allergen-specific serum IgE to a common inhalant and allergens with the ImmunoCAP System (Thermo Fisher/Phadia AB, Uppsala, Sweden).

In the GINIplus and LISAplus cohorts, all participants who were still in the study at ages 6, 10 and 15 years were invited for medical examinations including collection of blood samples. All blood samples were analyzed for allergen-specific serum IgE to common inhalant and food allergens with the CAP-RAST FEIA system (Pharmacia Diagnostics, Freiburg, Germany).

In the PIAMA cohort, clinical examinations including collection of blood samples were performed the ages of 4, 8, and 12 years. At age 4, all children with atopic mothers and a random sample of children with non-atopic mothers were invited. At ages 8 and 12 years, all participants that were still in the study, were invited. Blood samples were analysed for allergen-specific serum IgE to common inhalant and food allergens with the radioallergosorbent test-like method used at the Sanquin Laboratories (Amsterdam, The Netherlands).

Supplementary Table 2 provides an overview of the measurements of specific IgE against inhalant allergens in the different cohorts.

Land-Use Regression model development

Linear regression models were developed to maximize the adjusted explained variance, using a supervised stepwise selection procedure, first evaluating univariate regressions of the corrected annual average concentrations with all available potential predictors following procedures used before.[1,2] The predictor giving the highest adjusted explained variance (adjusted R^2) was selected for inclusion in the model if the direction of effect was as defined a priori. We then evaluated which of the remaining predictor variables further improved the model adjusted R^2, selected the one giving the highest gain in adjusted R^2, and the right direction of effect. Subsequent variables were not selected if they changed the direction of effect of one of the previously included variables. This process continued until there were no more variables with the right direction of effect, which added at least 0.01 (1%) to the adjusted R^2 of the previous model.

Results

In GINI/LISA South, participants with highly educated parents were over-represented in our study sample as compared to the full cohort. Participants of the most recent follow-up (between 51% of the baseline population in LISA North and 78% of the baseline population in BAMSE), more often had highly educated parents in all cohorts, and more often had parents with asthma and/or hay fever in BAMSE and GINI/LISA North (data not shown) as compared to non-participants. Children of highly educated parents and parents with asthma and/or hay fever were overrepresented among children with measurements of specific IgE in all cohorts except BAMSE (data not shown).

References

1. Beelen R, Hoek G, Vienneau D, Eeftens M, Dimakopoulou K, Pedeli X, et al. Development of NO2 and NOx land use regression models for estimating air pollution exposure in 36 study areas in Europe - The ESCAPE project. *Atmos Environ*. 2013; **72**: 10-23.

2. Eeftens M, Beelen R, de Hoogh K, Bellander T, Cesaroni G, Cirach M, et al. Development of Land Use Regression Models for PM2.5, PM2.5 Absorbance, PM10 and PMcoarse in 20 European Study Areas; Results of the ESCAPE Project. *Environ Sci Technol*. 2012; **46**(20): 11195-205.

Supplementary Table 1. Overview of cohort follow-ups.

Cohort	N at birth	Age (years)
BAMSE	4,089	< 1, 1, 2, 4, 8, 12, 16
GINIplus	5,991	< 1, 1, 2, 3, 4, 6, 10, 15
LISAplus	3,097	< 1, 1, 1.5, 2, 4, 6, 10, 15
PIAMA	3,963	< 1, 1, 2, 3, 4, 5, 6, 7, 8, 11, 14

Supplementary Table 2. Land-use regression models with model R^2.

Pollutant Cohort	Land-use regression model	Model R^2
NO_2		
BAMSE	5.82 + 1.08$\times10^{-3}$×ROADLENGTH_500 + 4.01$\times10^{-4}$×TRAFNEAR + 5.39$\times10^{-3}$×POP_100	82%
GINI/LISA North	19.66 + 3.48$\times10^{-7}$×INDUSTRY_5000 + 2.24$\times10^{-2}$×POP_100 + 4.10$\times10^{-6}$×PORT_5000 + 1.31$\times10^{-6}$×TRAFLOAD_100	89%
GINI/LISA South	7.43 + 1.98$\times10^{-6}$×TRAFLOAD_50 + 1.35$\times10^{-3}$×INTMAJORINVDIST + 2.37$\times10^{-2}$×ROADLENGTH_50 + 1.47$\times10^{-5}$×POP_5000 + 4.15$\times10^{-2}$×MAJORROADLENGTH_50 + 9.85×HLDRES_500	86%
PIAMA	- 7.80 + 1.18×REGIONALESTIMATE + 2.30$\times10^{-5}$×POP_5000 + 2.46$\times10^{-6}$×TRAFLOAD_50 + 1.06$\times10^{-4}$×ROADLENGTH_1000 + 9.84$\times10^{-5}$×HEAVYTRAFLOAD_25 + 12.19×DISTINVNEARC1 + 4.47$\times10^{-7}$×HEAVYTRAFLOAD_25_500	86%
$PM_{2.5}$ absorbance		
BAMSE	0.51 + 5.59$\times10^{-5}$×ROADLENGTH_500 + 2.55$\times10^{-6}$×HEAVYTRAFLOAD_50–8.38$\times10^{-9}$×WATER_5000	89%
GINI/LISA North	0.97 + 1.80$\times10^{-6}$×HEAVYTRAFLOAD_100 + 2.31$\times10^{-8}$×HEAVYTRAFLOAD_100_1000 + 1.64$\times10^{-8}$×INDUSTRY_5000 + 2.21$\times10^{-5}$×POP_1000	97%
GINI/LISA South	1.34 + 1.77$\times10^{-7}$×TRAFLOAD_50 + 1.84$\times10^{-3}$×ROADLENGTH_50 + 2.16$\times10^{-4}$×TRAFMAJORLOAD_1000	81%
PIAMA	0.07 + 2.95$\times10^{-9}$×TRAFLOAD_500 + 2.93$\times10^{-3}$×MAJORROADLENGTH_50 + 0.85×REGIONALESTIMATE + 7.90$\times10^{-9}$×HLDRES_5000 + 1.72$\times10^{-6}$×HEAVYTRAFLOAD_50	92%
$PM_{2.5}$		
BAMSE	7.95–8.96$\times10^{-6}$×WATER_500–1.48$\times10^{-7}$×WATER_500_5000 + 1.37$\times10^{-5}$×HEAVYTRAFLOAD_50 + 3.66$\times10^{-4}$×ROADLENGTH_500	87%
GINI/LISA North	81.73 + 5.61$\times10^{-8}$×HEAVYTRAFLOAD_1000 + 1.20$\times10^{-7}$×INDUSTRY_5000 + 1.04$\times10^{-4}$×POP_1000–2.57$\times10^{-5}$×XCOORD	88%
GINI/LISA South	11.90 + 1.94$\times10^{-2}$×MAJORROADLENGTH_50 + 4.95$\times10^{-4}$×ROADLENGTH_300–14.30×URBGREEN_5000 + 7.41$\times10^{-9}$×TRAFMAJORLOAD_1000	78%
PIAMA	9.46 + 0.42×REGIONALESTIMATE + 0.01×MAJORROADLENGTH_50 + 2.28$\times10^{-9}$×TRAFMAJORLOAD_1000	67%
PM_{10}		
BAMSE	6.01 + 5.26$\times10^{-6}$×TRAFLOAD_50 + 3.74$\times10^{-5}$×HLDRES_300	82%
GINI/LISA North	23.86 + 1.47$\times10^{-7}$×HEAVYTRAFLOAD_1000 + 2.44$\times10^{-4}$×POP_100	83%
GINI/LISA South	18.47 + 3.89$\times10^{-2}$×MAJORROADLENGTH_50–56.65×NATURAL_100 + 2.07$\times10^{-2}$×ROADLENGTH_50	69%
PIAMA	23.71 + 2.16$\times10^{-8}$×TRAFMAJORLOAD_500 + 6.68$\times10^{-6}$×POP_5000 + 0.02×MAJORROADLENGTH_50	68%
PM_{coarse}		
BAMSE	0.70 + 4.32$\times10^{-6}$×TRAFLOAD_50 + 2.73$\times10^{-5}$×HLDRES_300	72%
GINI/LISA North	7.42 + 2.14$\times10^{-4}$×MAJORROADLENGTH_1000–2.42$\times10^{-5}$×URBGREEN_300 + 1.36$\times10^{-7}$×INDUSTRY_5000	66%
GINI/LISA South	4.09 + 2.46$\times10^{-2}$×MAJORROADLENGTH_50d + 4.20$\times10^{-6}$×POP_5000 + 1.16$\times10^{-2}$×ROADLENGTH_50d	81%
PIAMA	7.59 + 5.02$\times10^{-9}$×TRAFLOAD_1000 + 1.38$\times10^{-7}$×PORT_5000 + 5.38$\times10^{-5}$×TRAFNEAR	51%

DISTINVNEARC1: Inverse distance to the nearest road; HLDRES_X: Sum of high density and low density residential land in X m buffer; HEAVYTRAFLOAD_X: Total heavy-duty traffic load of all roads in a buffer (sum of (heavy-duty traffic intensity *length of all segments)); INDUSTRY_X: industry in X m buffer; INTMAJORINVDIST: the product of inverse distance to the nearest major road and the traffic intensity on the nearest major road; MAJORROADLENGTH_X; Road length of major roads in X m buffer; NATURAL_X: natural land in X m buffer; POP_X: Number of inhabitants in X m buffer; PORT_X; port in X m buffer; REGIONALESTIMATE: Regional estimate; ROADLENGTH_X: Road length of major roads in X m buffer; TRAFNEAR: Traffic intensity on nearest road; TRAFLOAD_X: Total traffic load of all roads in X m buffer

(sum of (traffic intensity * length of all segments)); TRAFMAJORLOAD_X: Total traffic load of major roads in X m buffer (sum of (traffic intensity * length of all segments)); URBGREEN_X: urban green space in X m buffer; WATER_X: water in X m buffer; XCOORD: X-coordinate;

Supplementary Table 3. Measurements of specific IgE against inhalant allergens in the cohorts.

Cohort	Age (years)	Specific IgE against inhalant allergens
BAMSE	4	*Dermatophagoides pteronyssinus,* cat, dog, birch, *Cladosporium herbarum*
	8	*Dermatophagoides pteronyssinus,* cat, dog, birch, *Cladosporium herbarum*
	16	*Dermatophagoides pteronyssinus, Dermatophagoides farinae,* cat, dog, birch, *Cladosporium herbarum*
GINIplus & LISAplus	6	*Dermatophagoides pteronyssinus* , cat, dog, birch, *Cladosporium herbarum*
	10	*Dermatophagoides pteronyssinus* , cat, dog, birch, *Cladosporium herbarum*
	15	*Dermatophagoides pteronyssinus* , cat, dog, birch, *Cladosporium herbarum*
PIAMA	4	*Dermatophagoides pteronyssinus*, cat, dog, *Dactylis glomerata*, birch, *Alternaria alternata*
	8	*Dermatophagoides pteronyssinus*, cat, dog, *Dactylis glomerata*, birch, *Alternaria alternata*
	12	*Dermatophagoides pteronyssinus*, cat, *Dactylis glomerata*, birch

Supplementary Table 4. Distribution of estimated annual average air pollution levels at the participants' home addresses.

	BAMSE				GINI/LISA North				GINI/LISA South				PIAMA			
Pollutant	**Mean (Std)**	**Min**	**P50**	**Max**	**Mean (Std)**	**Min**	**P50**	**Max**	**Mean (Std)**	**Min**	**P50**	**Max**	**Mean (Std)**	**Min**	**P50**	**Max**
Birth address		**N = 4008**				**N = 2684**				**N = 3549**				**N = 3844**		
NO_2 [μg/m³]	14·1 (5·4)	6·0	12·5	33·0	23·8 (3·6)	19·7	23·2	62·8	21·8 (6·1)	11·5	20·8	61·1	23·2 (6·6)	8·7	23·2	59·6
$PM_{2·5}$ abs [$10^{-5}m^{-1}$]	0·7 (0·2)	0·4	0·6	1·3	1·2 (0·2)	1·0	1·2	3·1	1·7 (0·2)	1·3	1·7	3·6	1·2 (0·2)	0·8	1·2	3·0
$PM_{2·5}$ [μg/m³]	7·8 (1·2)	4·2	8·1	11·4	17·4 (0·7)	15·8	17·2	21·5	13·4 (1·0)	10·6	13·4	18·3	16·4 (0·7)	15·3	16·5	21·1
PM_{10} [μg/m³]	15·7 (3·8)	6·0	15·5	30·9	25·5 (1·2)	23·9	25·2	33·9	20·4 (2·4)	14·8	20·4	34·4	25·0 (1·2)	23·7	24·7	33·2
PM_{coarse} [μg/m³]	7·9 (3·0)	0·7	7·7	20·2	8·5 (0·7)	1·9	8·4	13·9	6·8 (1·5)	4·1	6·5	16·0	8·4 (0·8)	7·6	8·1	14·0
Latest address [a]		**N = 2834**				**N = 1779** [b]				**N = 2411**				**N = 2291**		
NO_2[μg/m³]	11·7 (5·8)	3·6	9·4	60·9	23·6 (3·1)	19·7	23·2	59·8	19·8 (5·1)	11·5	18·8	58·0	21·6 (6·0)	9·2	21·8	53·5
$PM_{2·5}$ abs [$10^{-5}m^{-1}$]	0·6 (0·2)	0·3	0·6	2·2	1·2 (0·2)	1·0	1·2	3·1	1·6 (0·1)	1·3	1·6	3·2	1·2 (0·2)	0·8	1·2	2·1
$PM_{2·5}$ [μg/m³]	7·4 (1·7)	4·2	7·2	24·7	17·4 (0·7)	15·8	17·3	21·4	13·3 (0·9)	10·7	13·2	18·8	16·3 (0·6)	14·9	16·5	19·3
PM_{10} [μg/m³]	15·1 (4·0)	6·0	14·6	53·7	25·5 (1·2)	23·9	25·2	32·7	20·0 (2·3)	14·8	20·4	32·0	24·7 (1·0)	23·7	24·5	30·5
PM_{coarse} [μg/m³]	7·1 (2·8)	0·7	6·6	34·0	8·5 (0·7)	1·9	8·4	13·8	6·3 (1·3)	4·1	6·1	14·4	8·2 (0·7)	7·6	8·0	11·4

[a] age 16 for BAMSE, age 15 for GINI/LISA, and age 14 for PIAMA
[b] N=1784 for PM_{coarse}

Supplementary Table 5. Adjusted [a] associations of air pollution exposure with asthma and rhinoconjunctivitis from meta-analyses with I^2 statistics and p-values of tests for heterogeneity of cohort-specific estimates (p_{het}).

	Asthma						Rhinitis					
	Incidence			Prevalence			Incidence			Prevalence		
Pollutant [increment]	**OR**	**(95% CI)**	**I^2 (p_{het})**	**OR**	**(95% CI)**	**I^2 (p_{het})**	**OR**	**(95% CI)**	**I^2 (p_{het})**	**OR**	**(95% CI)**	**I^2 (p_{het})**
Birth address												
NO_2 [10 µg/m³]	1·13	(1·02-1·25)	0·0 (0·399)	1·06	(0·88-1·26)	46·6 (0·132)	1·03	(0·85-1·23)	69·1 (0·021)	1·07	(0·87-1·31)	73·3 (0·010)
$PM_{2·5}$ abs [1 $10^{-5}m^{-1}$]	1·29	(1·00-1·66)	0·0 (0·797)	1·24	(0·97-1·60)	0·0 (0·537)	0·81	(0·52-1·24)	61·8 (0·049)	0·91	(0·57-1·45)	67·5 (0·026)
$PM_{2·5}$ [5 µg/m³]	1·25	(0·94-1·66)	0·0 (0·504)	1·34	(1·00-1·79)	0·0 (0·822)	1·03	(0·65-1·62)	61·2 (0·052)	1·05	(0·67-1·65)	56·3 (0·076)
PM_{10} [10 µg/m³]	1·08	(0·77-1·51)	29·0 (0·238)	1·10	(0·74-1·63)	40·9 (0·166)	0·82	(0·64-1·07)	24·0 (0·267)	0·93	(0·62-1·40)	57·6 (0·070)
PM_{coarse} [5 µg/m³]	1·15	(0·83-1·59)	49·6 (0·114)	1·06	(0·80-1·39)	36·5 (0·193)	0·84	(0·68-1·03)	29·0 (0·238)	0·85	(0·68-1·08)	33·6 (0·211)
Current address												
NO_2 [10 µg/m³]	1·03	(0·88-1·19)	37·7 (0·186)	1·04	(0·93-1·16)	29·5 (0·235)	0·99	(0·76-1·28)	83·5 (0·000)	0·93	(0·74-1·19)	82·8 (0·001)
$PM_{2·5}$ abs [1 $10^{-5}m^{-1}$]	1·05	(0·72-1·52)	29·4 (0·236)	1·14	(0·91-1·43)	0·0 (0·413)	0·85	(0·50-1·46)	72·8 (0·012)	0·82	(0·49-1·36)	75·8 (0·006)
$PM_{2·5}$ [5 µg/m³]	1·13	(0·85-1·49)	5·0 (0·368)	1·18	(0·91-1·53)	14·2 (0·321)	1·30	(0·73-2·32)	75·2 (0·007)	1·12	(0·75-1·67)	58·4 (0·066)
PM_{10} [10 µg/m³]	0·91	(0·75-1·11)	0·0 (0·418)	1·03	(0·80-1·34)	20·1 (0·289)	1·05	(0·64-1·72)	69·8 (0·019)	1·01	(0·69-1·48)	60·6 (0·054)
PM_{coarse} [5 µg/m³]	1·06	(0·75-1·51)	44·0 (0·147)	1·00	(0·88-1·15)	4·3 (0·371)	0·96	(0·65-1·41)	65·9 (0·032)	0·96	(0·65-1·42)	70·1 (0·018)

[a] adjusted for sex, maternal and paternal asthma and hay fever, native nationality, parental education, breastfeeding, older siblings, day-care attendance, maternal smoking during pregnancy, parental smoking at home, mould/dampness at home, pets, use of gas for cooking, municipality (BAMSE only).

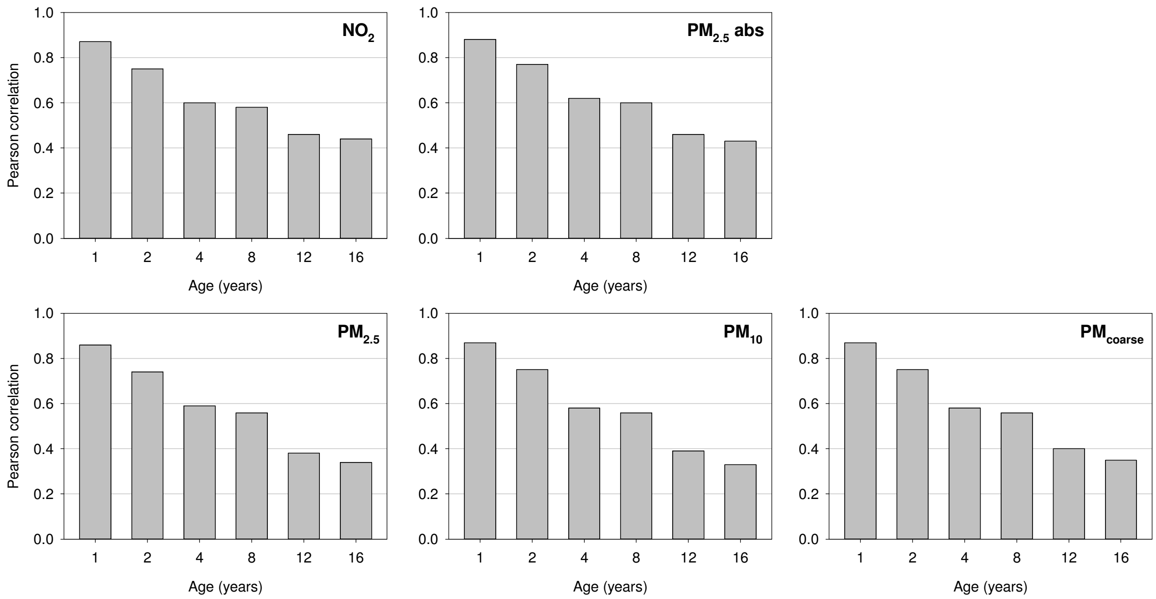
Supplementary Table 6. Adjusted [a] associations of air pollution exposure with asthma incidence and prevalence from meta-analyses with and without PIAMA.

	Incidence				Prevalence			
	All cohorts		Without PIAMA		All cohorts		Without PIAMA	
Pollutant [increment]	**OR**	**(95% CI)**	**OR**	**(95% CI)**	**OR**	**(95% CI)**	**OR**	**(95% CI)**
Birth address								
NO_2 [10 µg/m³]	1·13	(1·02-1·25)	1·02	(0·85-1·22)	1·06	(0·88-1·26)	0·97	(0·77-1·23)
$PM_{2.5}$ abs [1 $10^{-5}m^{-1}$]	1·29	(1·00-1·66)	1·10	(0·71-1·71)	1·24	(0·97-1·60)	1·02	(0·67-1·56)
$PM_{2.5}$ [5 µg/m³]	1·25	(0·94-1·66)	1·11	(0·79-1·54)	1·34	(1·00-1·79)	1·23	(0·87-1·75)
PM_{10} [10 µg/m³]	1·08	(0·77-1·51)	0·91	(0·75-1·11)	1·10	(0·74-1·63)	0·92	(0·74-1·15)
PM_{coarse} [5 µg/m³]	1·15	(0·83-1·59)	0·95	(0·82-1·09)	1·06	(0·80-1·39)	0·95	(0·82-1·10)
Current address								
NO_2 [10 µg/m³]	1·03	(0·88-1·19)	0·94	(0·80-1·09)	1·04	(0·93-1·16)	0·96	(0·67-1·36)
$PM_{2.5}$ abs [1 $10^{-5}m^{-1}$]	1·05	(0·72-1·52)	0·79	(0·51-1·22)	1·14	(0·91-1·43)	0·84	(0·37-1·87)
$PM_{2.5}$ [5 µg/m³]	1·13	(0·85-1·49)	1·01	(0·75-1·35)	1·18	(0·91-1·53)	1·47	(0·68-3·19)
PM_{10} [10 µg/m³]	0·91	(0·75-1·11)	0·87	(0·71-1·07)	1·03	(0·80-1·34)	1·13	(0·62-2·06)
PM_{coarse} [5 µg/m³]	1·06	(0·75-1·51)	0·92	(0·75-1·13)	1·00	(0·88-1·15)	0·85	(0·56-1·30)

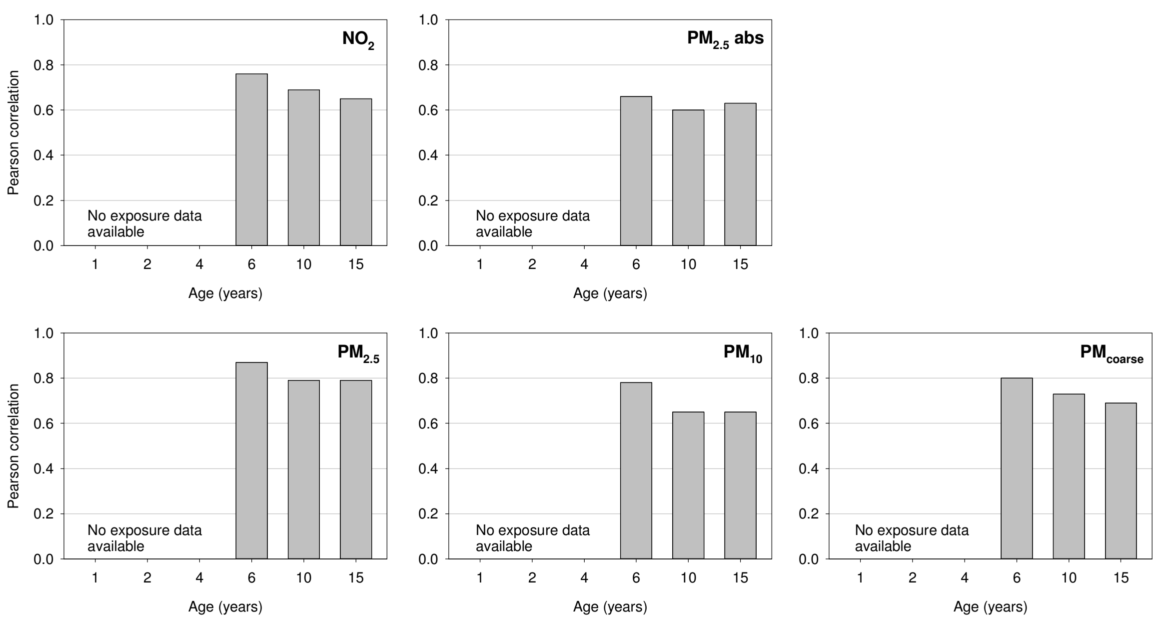
[a] adjusted for sex, maternal and paternal asthma and hay fever, native nationality, parental education, breastfeeding, older siblings, day-care attendance, maternal smoking during pregnancy, parental smoking at home, mould/dampness at home, pets, use of gas for cooking, municipality (BAMSE only).

Supplementary Figure 1. Correlation of birth address exposures with exposures at the different follow-up birth cohort.

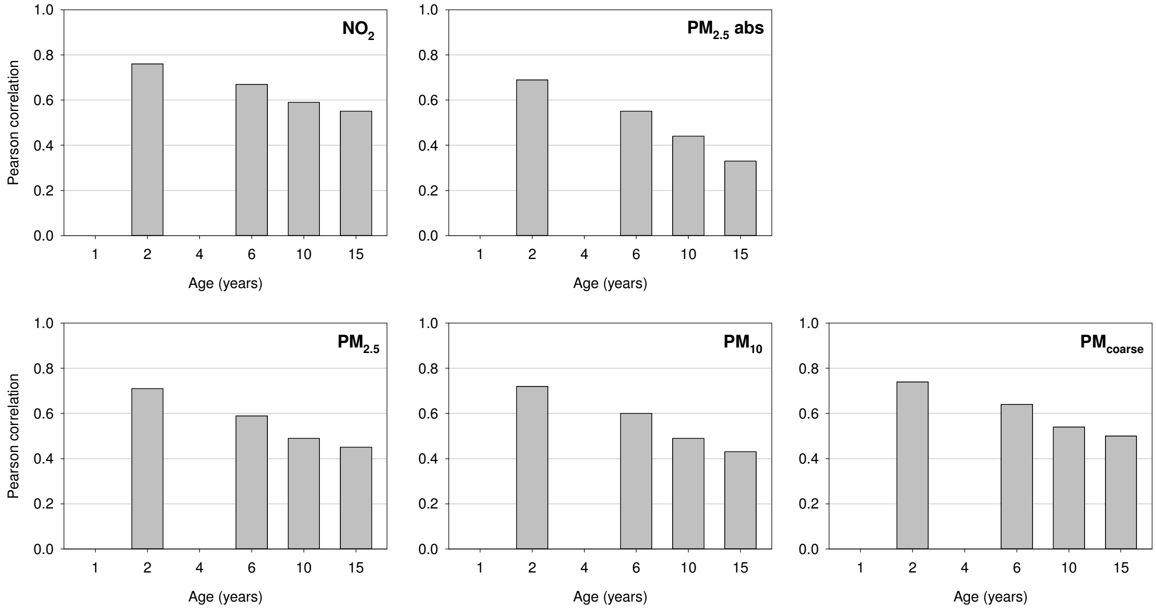
A) BAMSE



B) GINI/LISA North

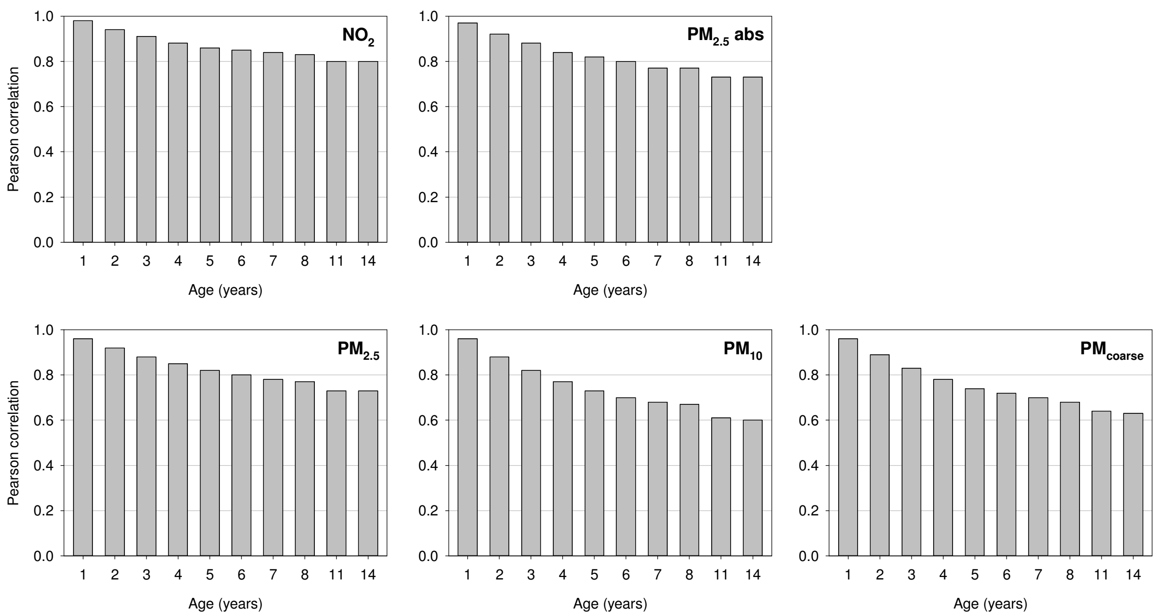


C) GINI/LISA South*

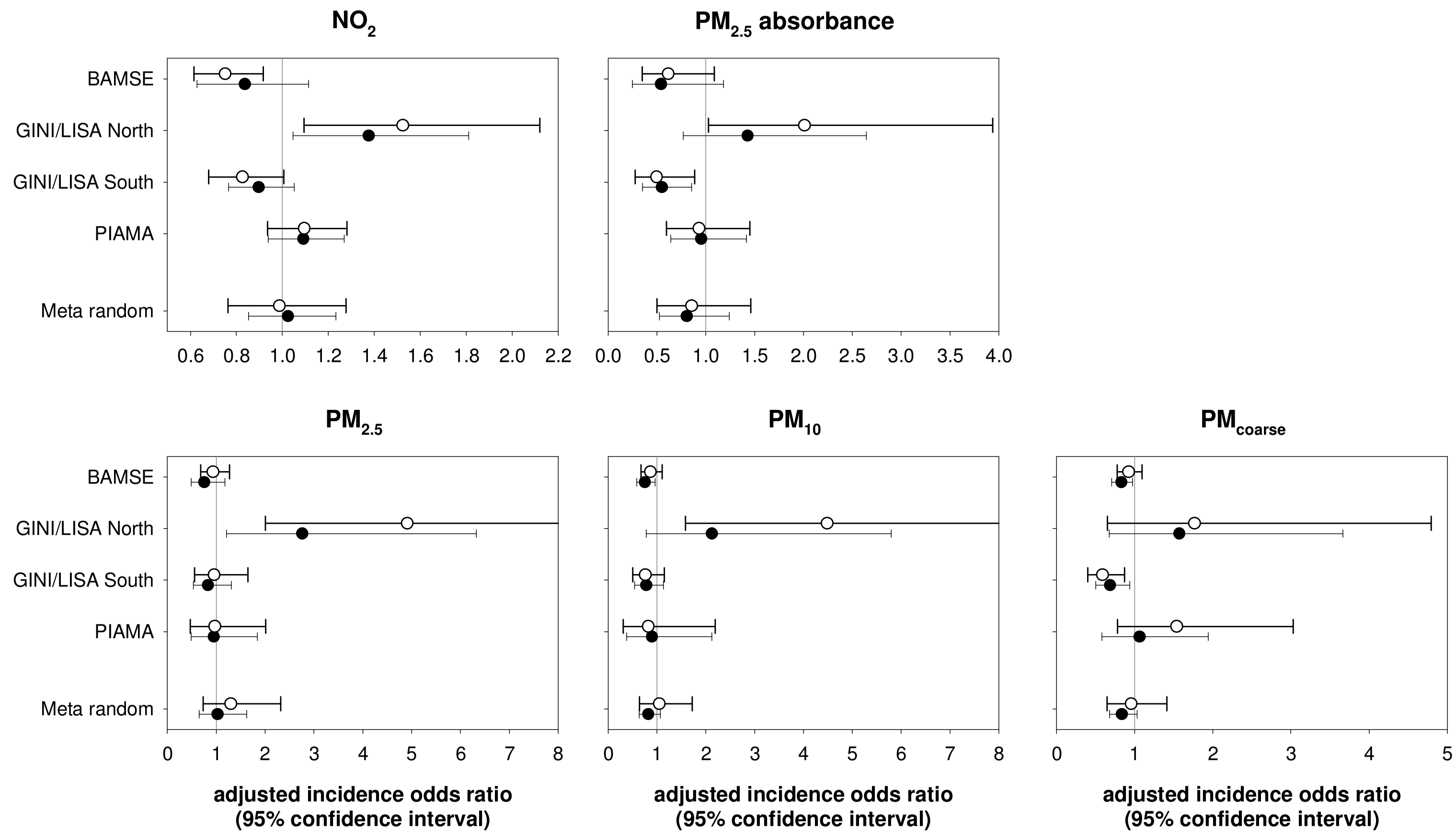


* No data available at 4 years.

D) PIAMA

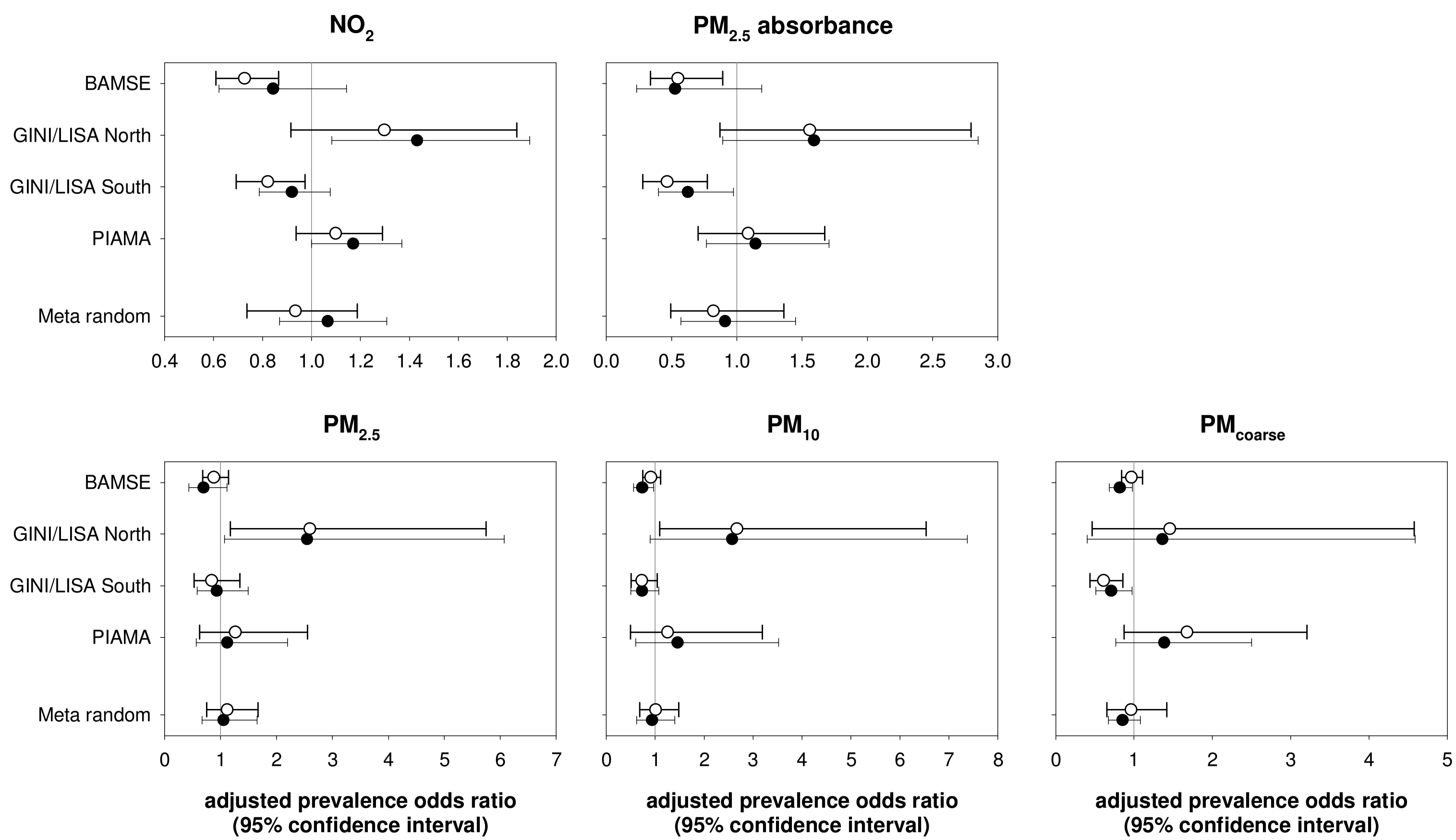


Supplementary Figure 2. Adjusted [a] cohort specific and combined (meta random) odds ratios of the associations of air pollution exposure with rhinoconjunctivitis incidence. Black dots represent associations with birth address exposure, white dots represent associations with current address exposure.



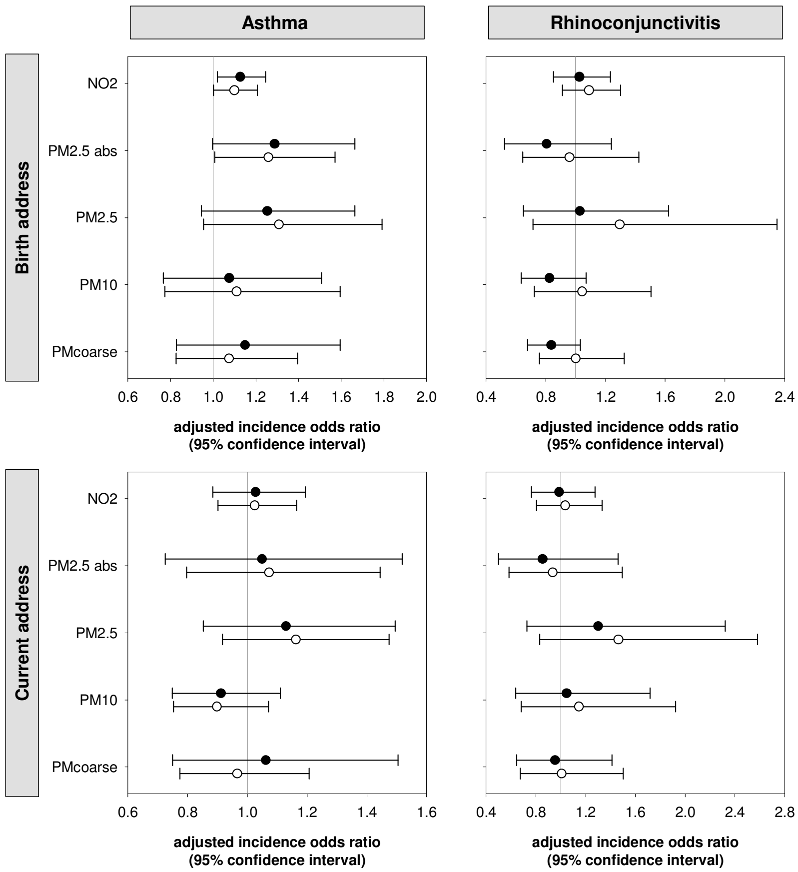
[a] adjusted for sex, maternal and paternal asthma and hay fever, native nationality, parental education, breastfeeding, older siblings, day-care attendance, maternal smoking during pregnancy, parental smoking at home, mould/dampness at home, pets, use of gas for cooking, and municipality (BAMSE only).

Supplementary Figure 3. Adjusted [a] cohort specific and combined (meta random) odds ratios of the associations of air pollution exposure with rhinoconjunctivitis prevalence. Black dots represent associations with birth address exposure, white dots represent associations with current address exposure.



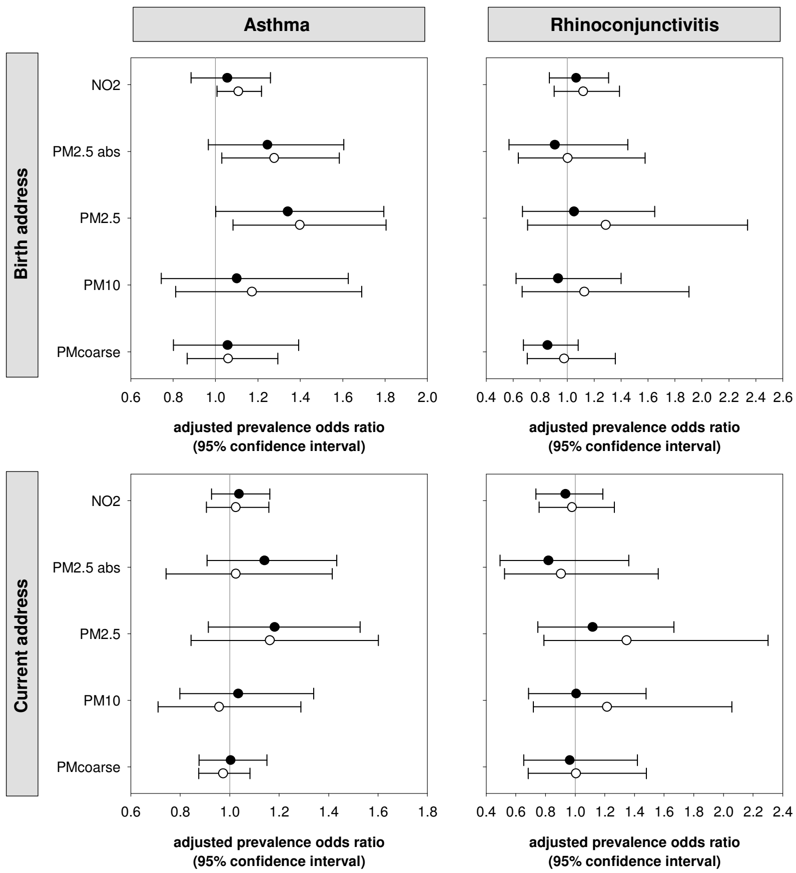
[a] adjusted for sex, maternal and paternal asthma and hay fever, native nationality, parental education, breastfeeding, older siblings, day-care attendance, maternal smoking during pregnancy, parental smoking at home, mould/dampness at home, pets, use of gas for cooking, and municipality (BAMSE only).

Supplementary Figure 4. Crude vs adjusted [a] odds ratios of the associations of air pollution exposure with asthma and rhinoconjunctivitis incidence from random effects meta-analysis. Black dots represent adjusted associations, white dots represent crude associations.



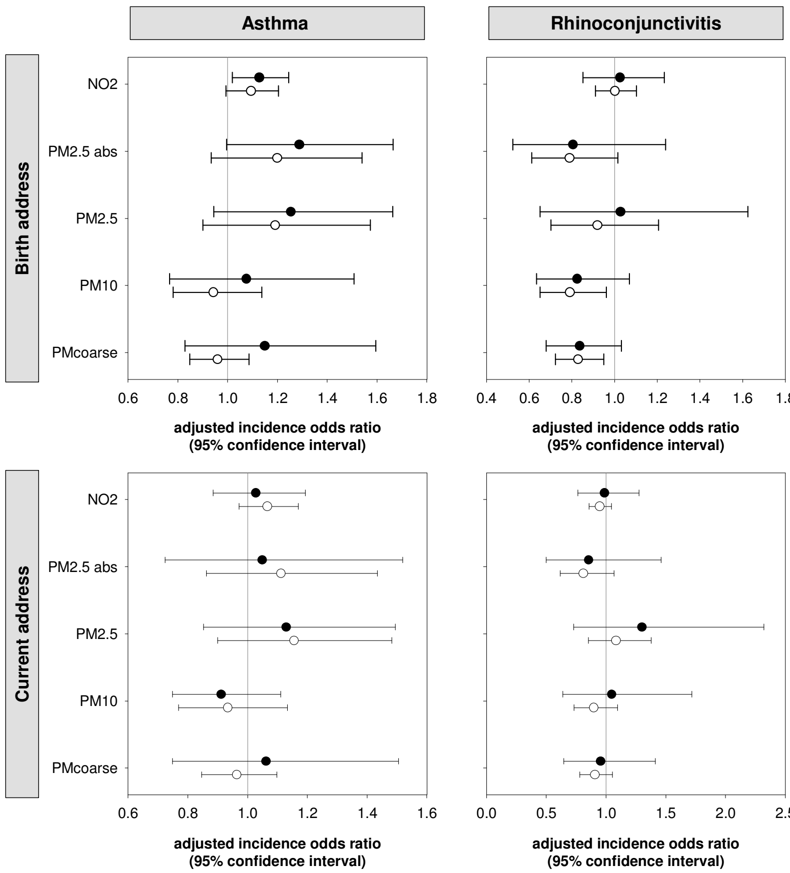
[a] adjusted for sex, maternal and paternal asthma and hay fever, native nationality, parental education, breastfeeding, older siblings, day-care attendance, maternal smoking during pregnancy, parental smoking at home, mould/dampness at home, pets, use of gas for cooking, and municipality (BAMSE only).

Supplementary Figure 5. Crude vs adjusted [a] odds ratios of the associations of air pollution exposure with asthma and rhinoconjunctivitis prevalence from random effects meta-analysis. Black dots represent adjusted associations, white dots represent crude associations.



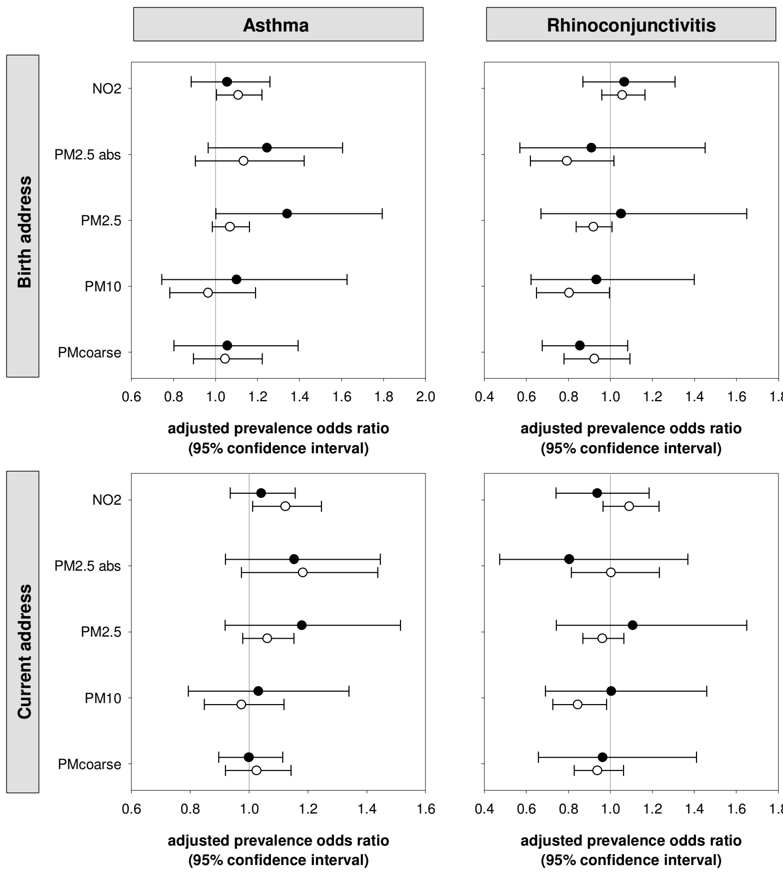
[a] adjusted for sex, maternal and paternal asthma and hay fever, native nationality, parental education, breastfeeding, older siblings, day-care attendance, maternal smoking during pregnancy, parental smoking at home, mould/dampness at home, pets, use of gas for cooking, and municipality (BAMSE only).

Supplementary Figure 6. Comparison of adjusted [a] odds ratios of the associations of air pollution exposure with asthma and rhinoconjunctivitis incidence from pooled analysis and random effects meta-analysis. Black dots represent associations from meta-analysis, white dots represent associations from pooled analysis.



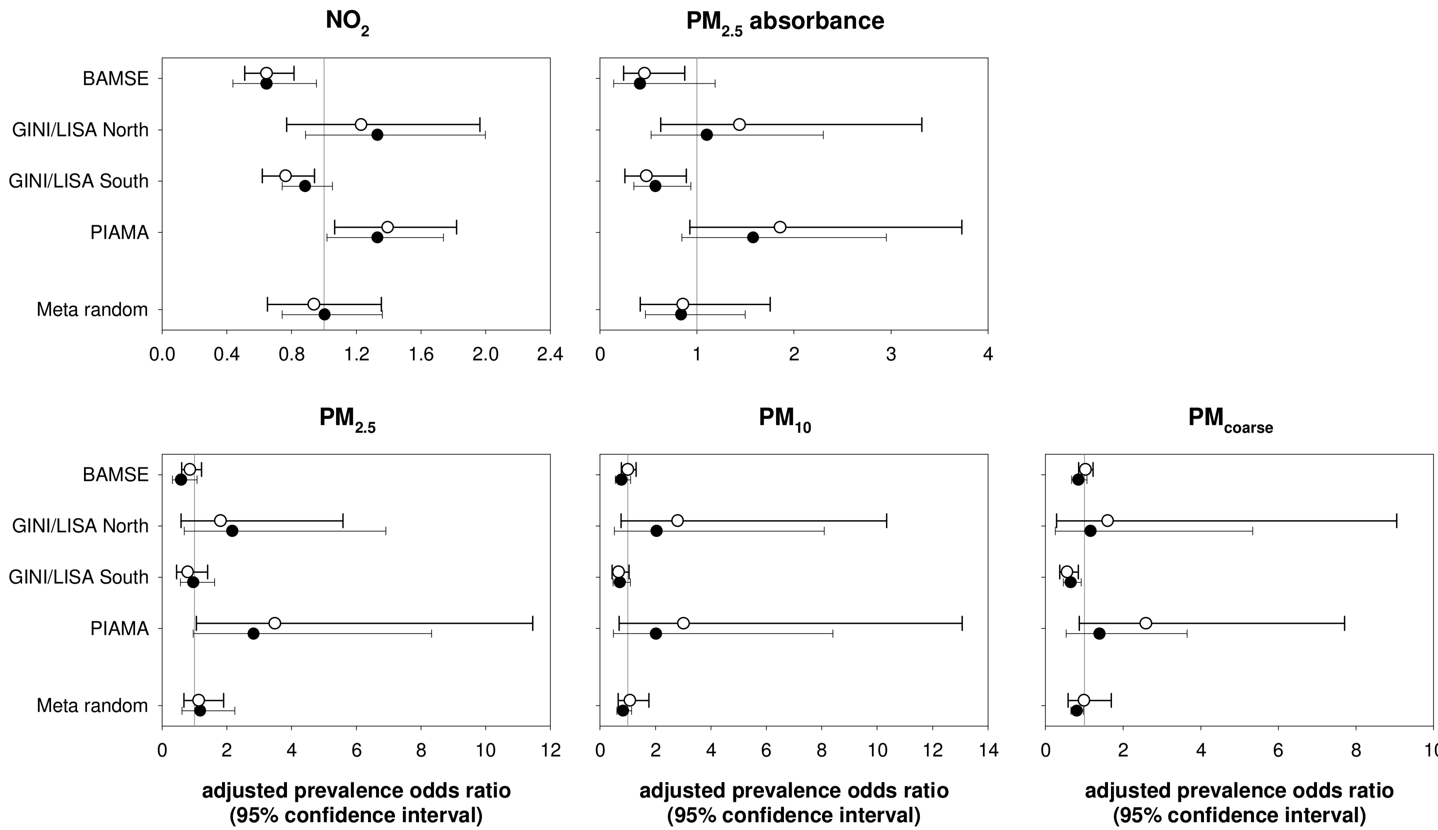
[a] adjusted for sex, maternal and paternal asthma and hay fever, native nationality, parental education, breastfeeding, older siblings, day-care attendance, maternal smoking during pregnancy, parental smoking at home, mould/dampness at home, pets, use of gas for cooking, and municipality (BAMSE only). Pooled analyses were additionally adjusted for cohort.

Supplementary Figure 7. Comparison of adjusted [a] odds ratios of the associations of air pollution exposure with asthma and rhinoconjunctivitis prevalence from pooled analysis and random effects meta-analysis. Black dots represent associations from meta-analysis, white dots represent associations from pooled analysis.



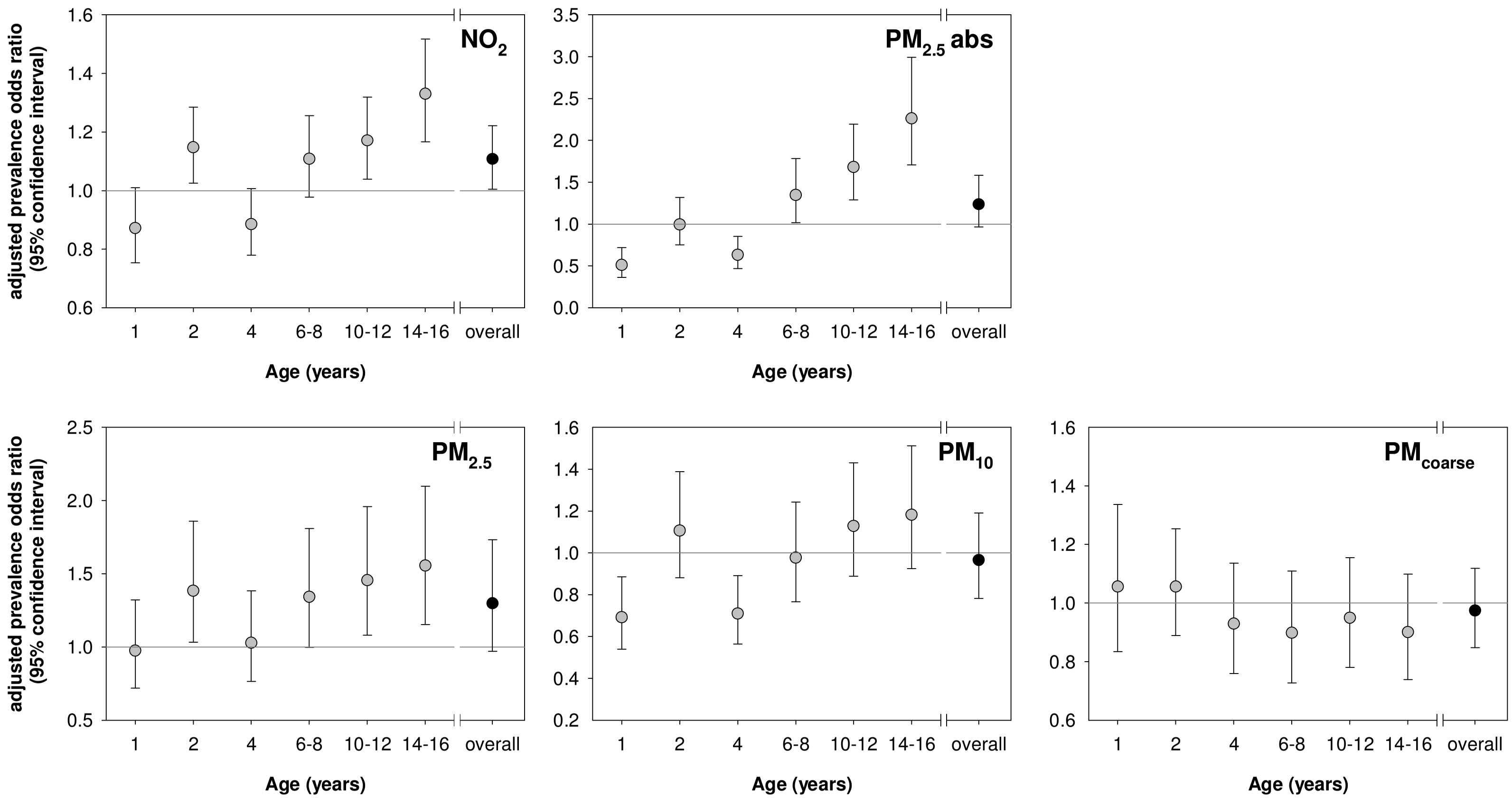
[a] adjusted for sex, maternal and paternal asthma and hay fever, native nationality, parental education, breastfeeding, older siblings, day-care attendance, maternal smoking during pregnancy, parental smoking at home, mould/dampness at home, pets, use of gas for cooking, and municipality (BAMSE only). Pooled analyses were additionally adjusted for cohort.

Supplementary Figure 8. Adjusted [a] cohort specific and combined (meta random) odds ratios of the associations of air pollution exposure with allergic rhinoconjunctivitis prevalence. Black dots represent associations with birth address exposure, white dots represent associations with current address exposure.



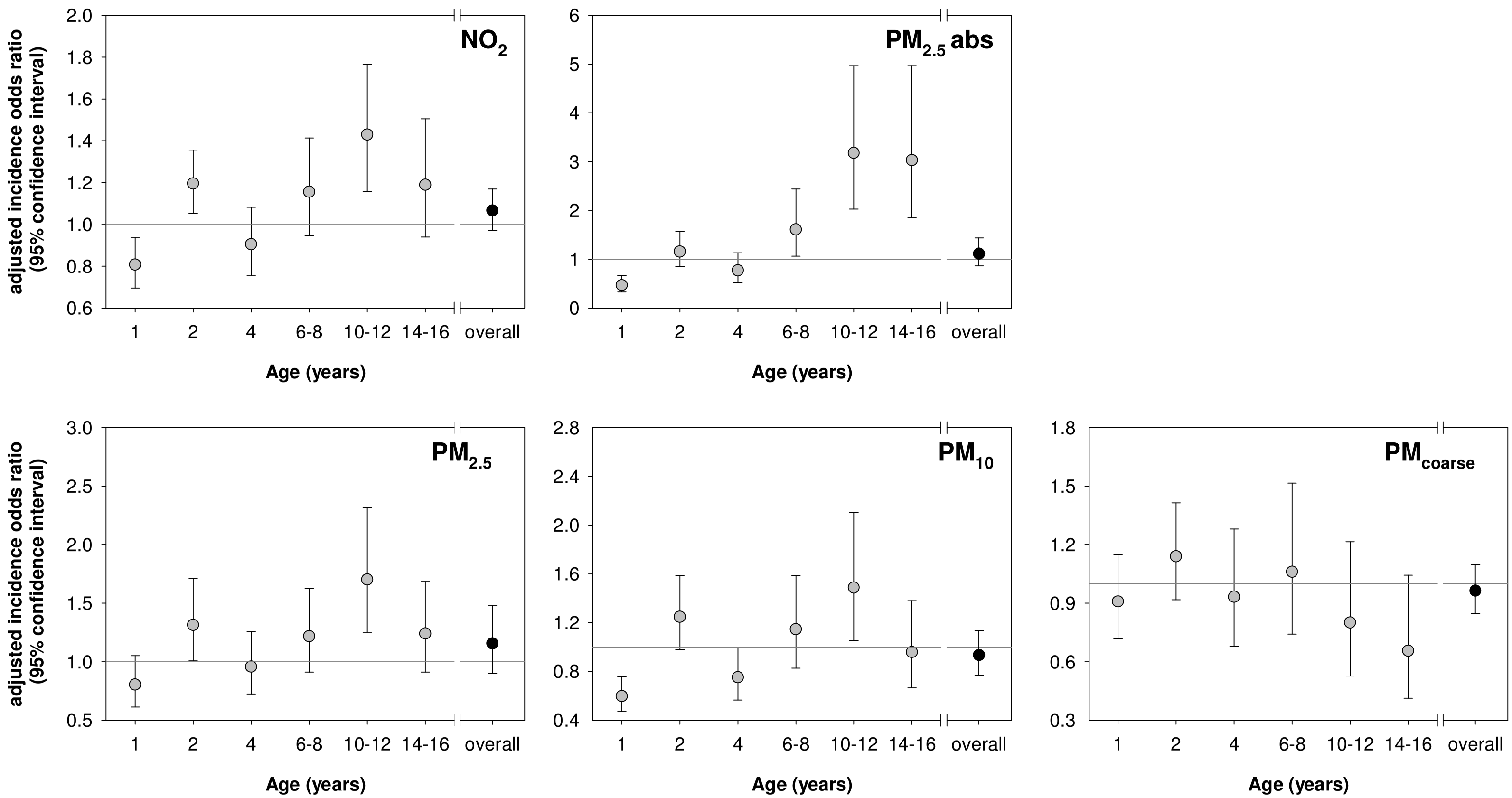
[a] adjusted for sex, maternal and paternal asthma and hay fever, native nationality, parental education, breastfeeding, older siblings, day-care attendance, maternal smoking during pregnancy, parental smoking at home, mould/dampness at home, pets, use of gas for cooking, and municipality (BAMSE only).

Supplementary Figure 9. Adjusted [a] age-specific odds ratios of the associations of air pollution exposure at the birth address with asthma prevalence from pooled analyses.



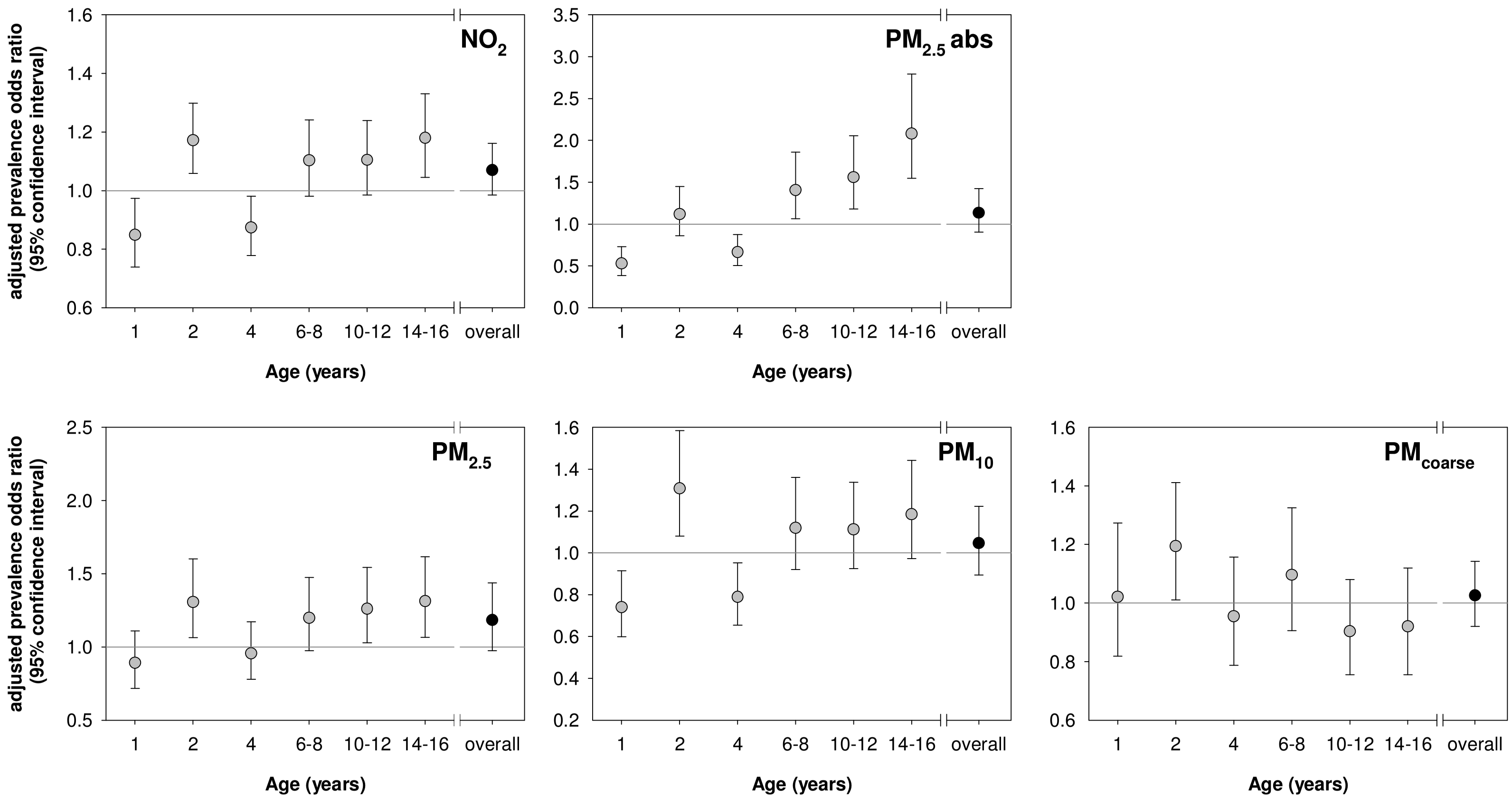
[a] adjusted for maternal and paternal asthma and hay fever, native nationality, parental education, breastfeeding, older siblings, day-care attendance, maternal smoking during pregnancy, parental smoking at home, mould/dampness at home, pets, use of gas for cooking, municipality (BAMSE only), and cohort.

Supplementary Figure 10. Adjusted [a] age-specific odds ratios of the associations of air pollution exposure at the current address with asthma incidence from pooled analyses.



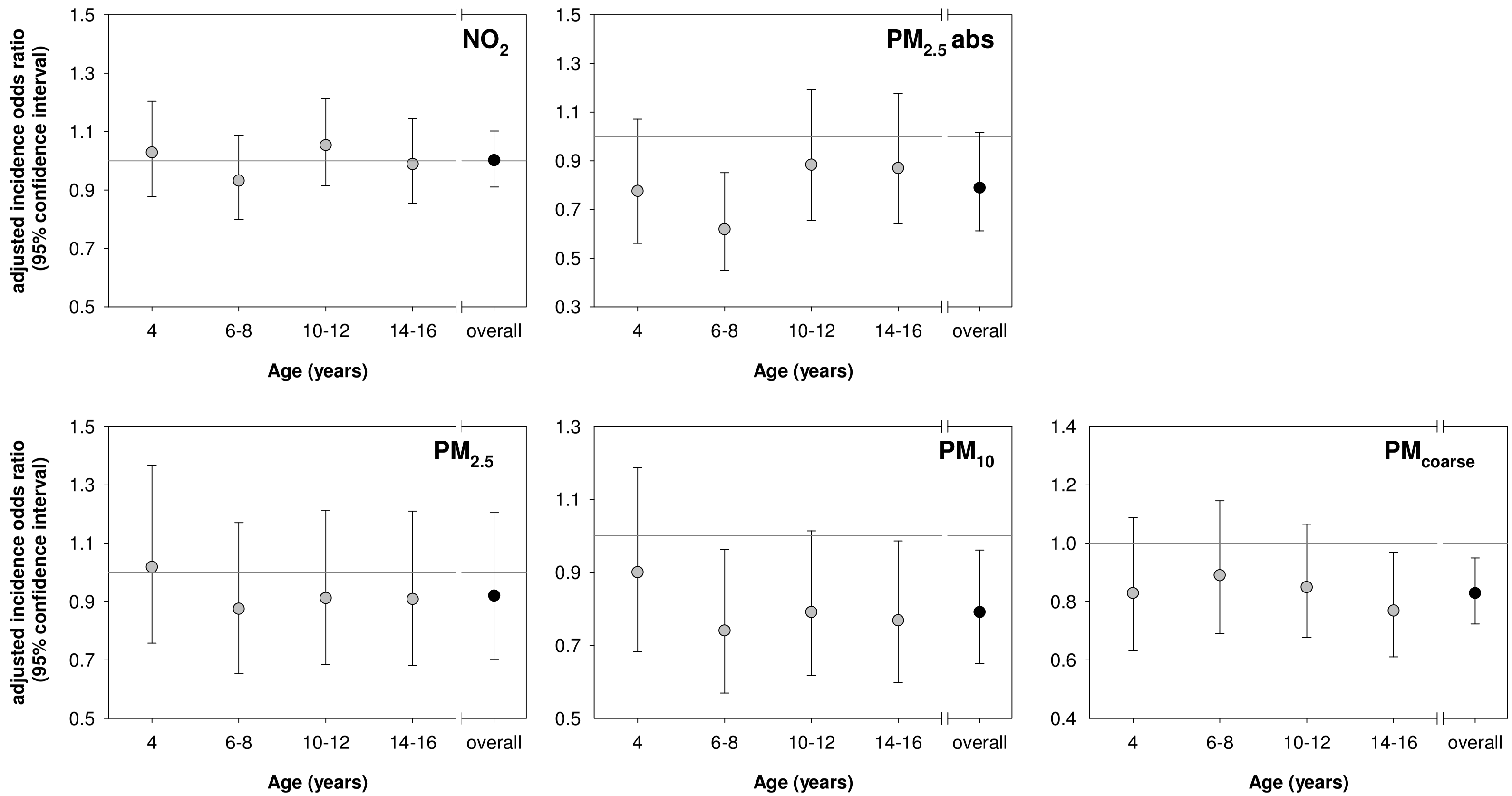
[a] adjusted for maternal and paternal asthma and hay fever, native nationality, parental education, breastfeeding, older siblings, day-care attendance, maternal smoking during pregnancy, parental smoking at home, mould/dampness at home, pets, use of gas for cooking, municipality (BAMSE only), and cohort.

Supplementary Figure 11. Adjusted [a] age-specific odds ratios of the associations of air pollution exposure at the current address with asthma prevalence from pooled analyses.



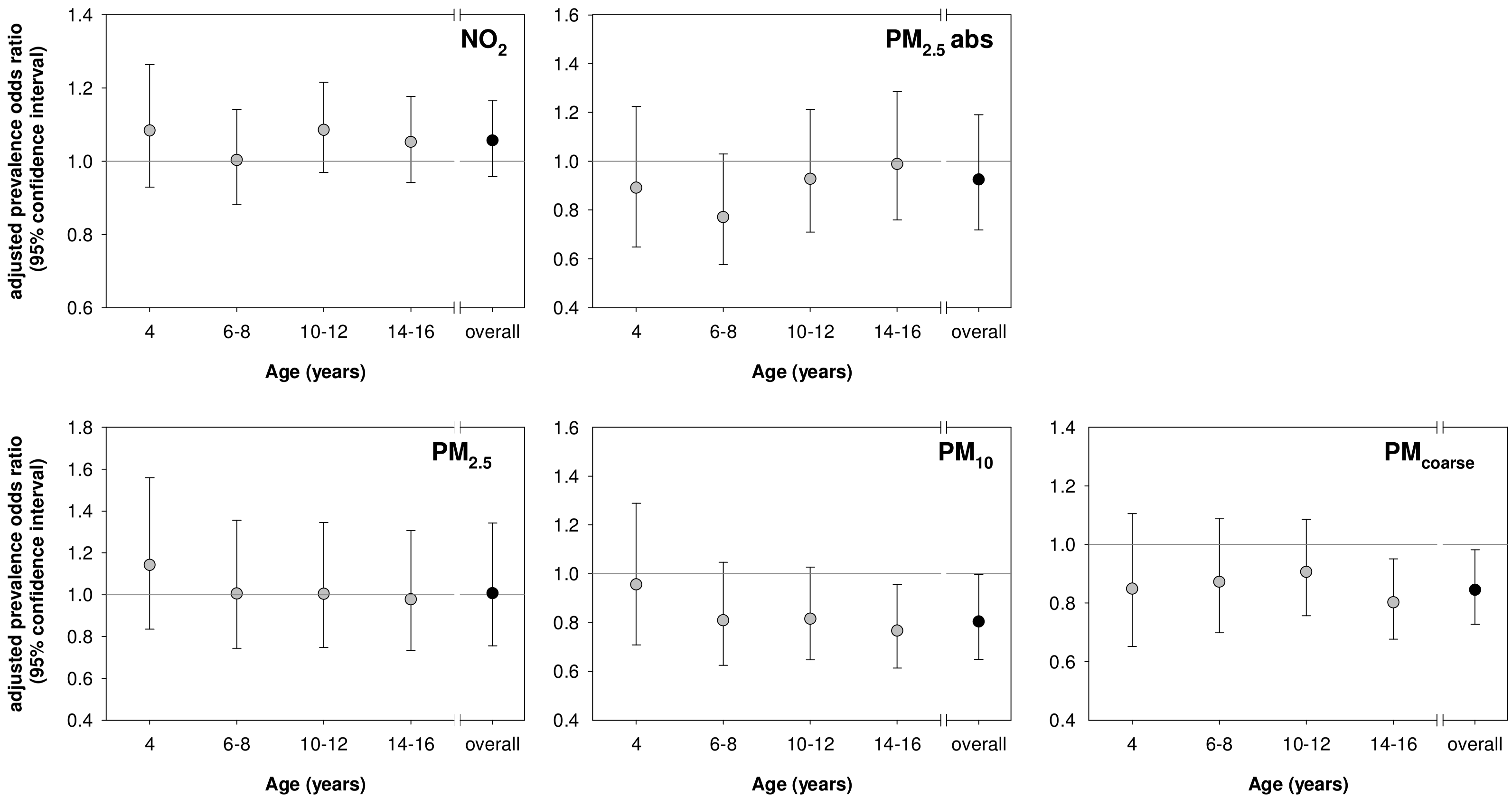
[a] adjusted for maternal and paternal asthma and hay fever, native nationality, parental education, breastfeeding, older siblings, day-care attendance, maternal smoking during pregnancy, parental smoking at home, mould/dampness at home, pets, use of gas for cooking, municipality (BAMSE only), and cohort.

Supplementary Figure 12. Adjusted [a] age-specific odds ratios of the associations of air pollution exposure at the birth address with rhinoconjunctivitis incidence from pooled analyses.



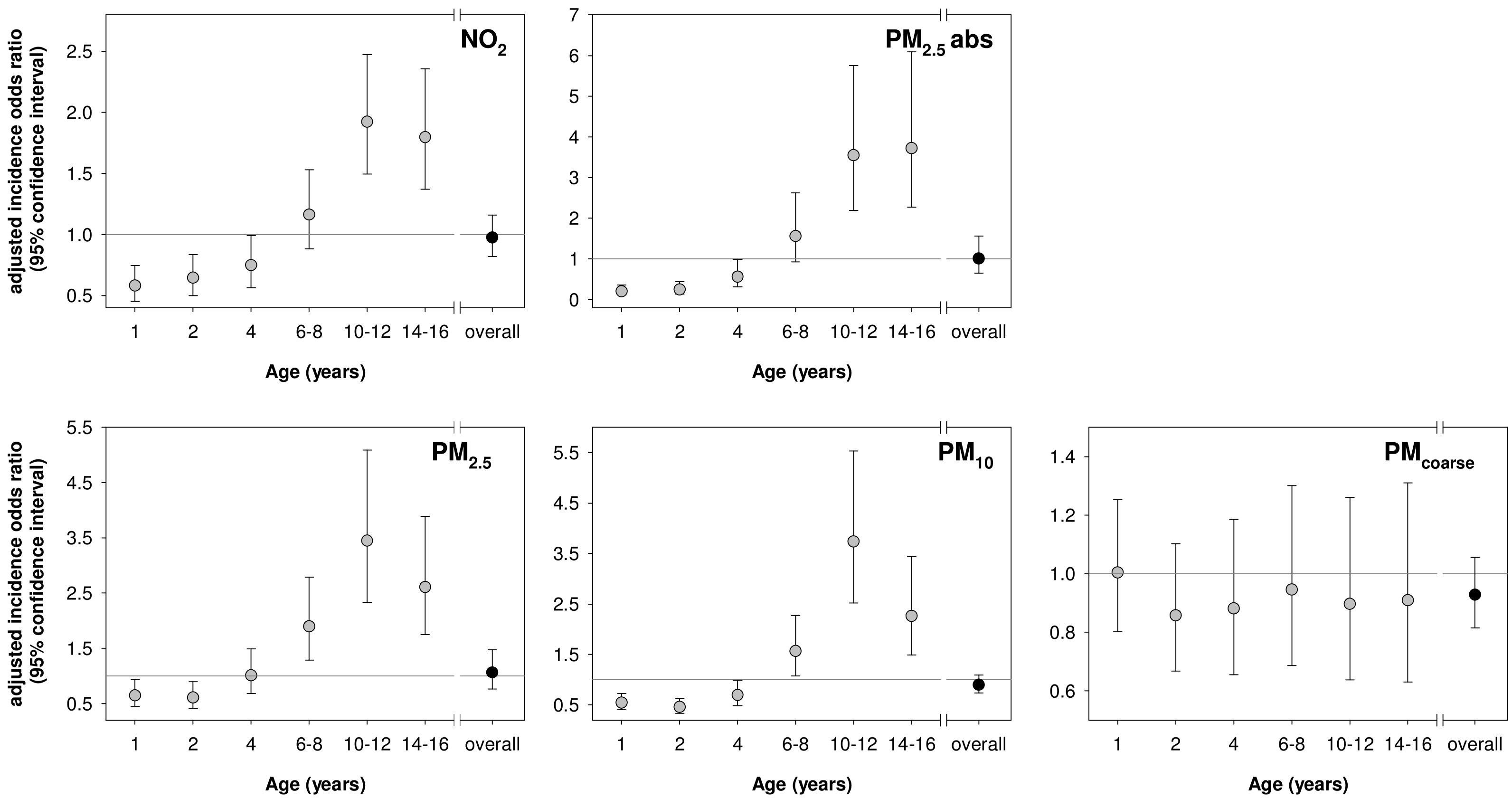
[a] adjusted for maternal and paternal asthma and hay fever, native nationality, parental education, breastfeeding, older siblings, day-care attendance, maternal smoking during pregnancy, parental smoking at home, mould/dampness at home, pets, use of gas for cooking, municipality (BAMSE only), and cohort.

Supplementary Figure 13. Adjusted [a] age-specific odds ratios of the associations of air pollution exposure at the birth address with rhinoconjunctivitis prevalence from pooled analyses.



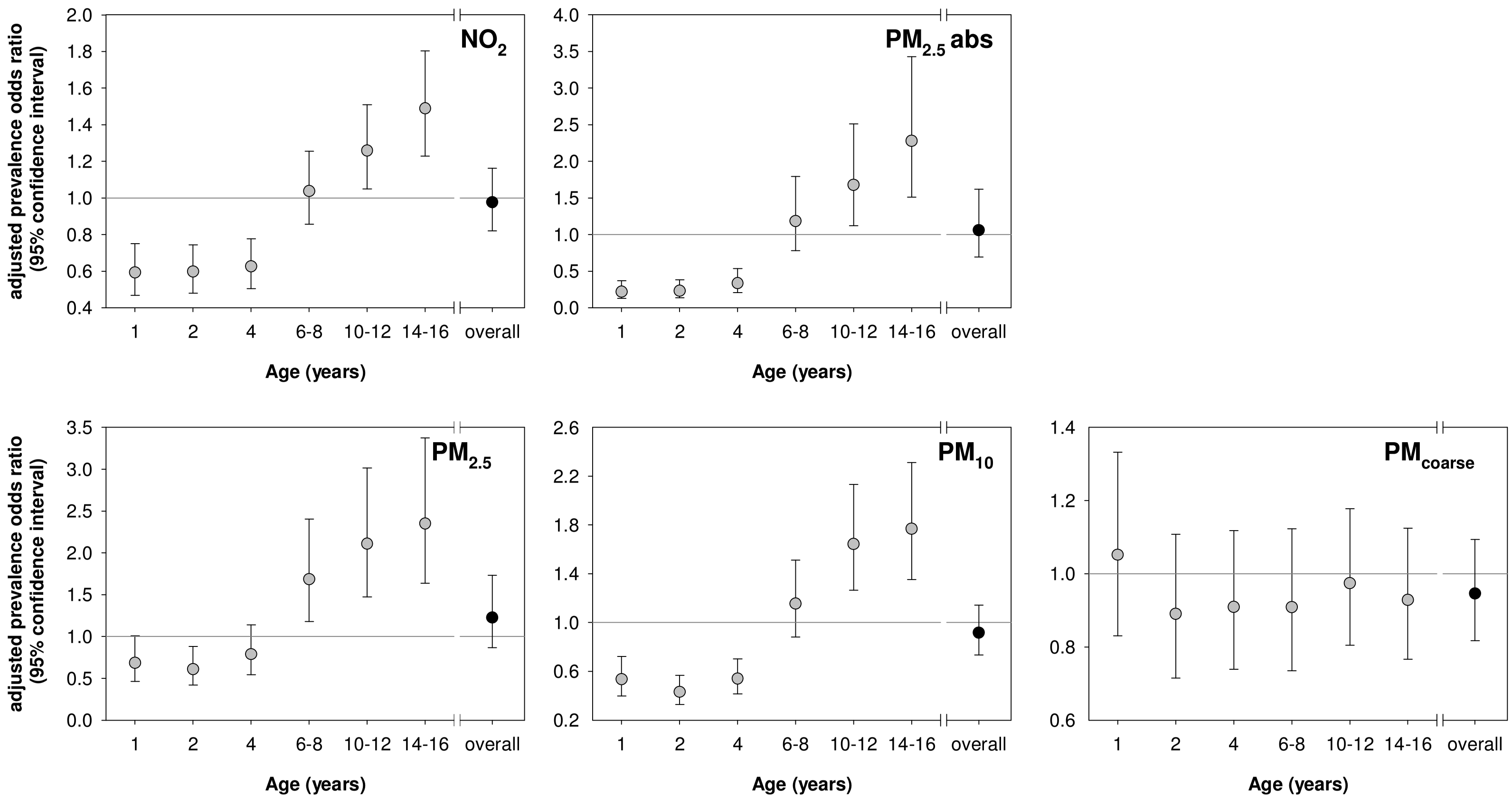
[a] adjusted for maternal and paternal asthma and hay fever, native nationality, parental education, breastfeeding, older siblings, day-care attendance, maternal smoking during pregnancy, parental smoking at home, mould/dampness at home, pets, use of gas for cooking, municipality (BAMSE only), and cohort.

Supplementary Figure 14. Adjusted [a] age-specific odds ratios of the associations of air pollution exposure at the birth address with asthma incidence excluding data from the PIAMA cohort.



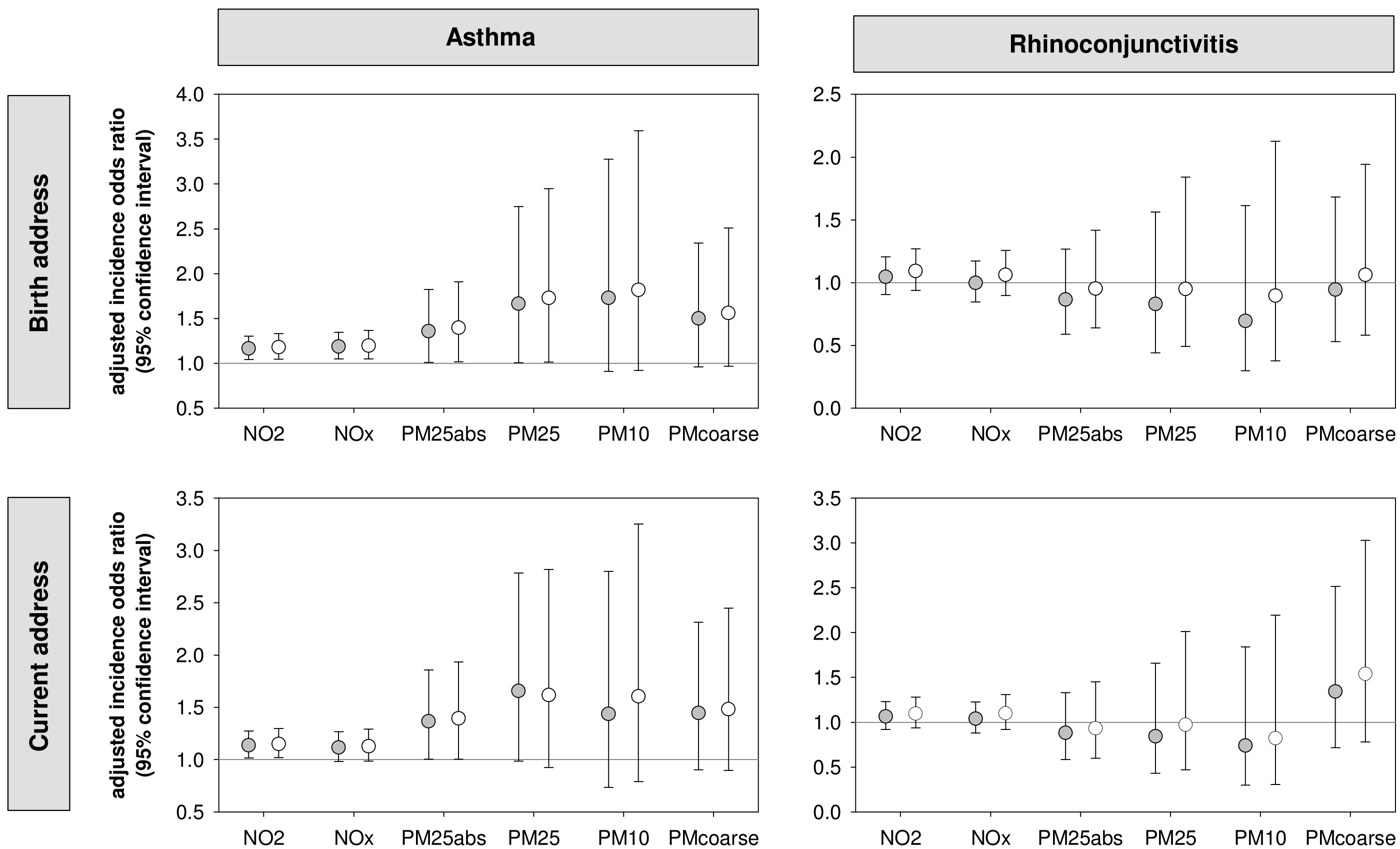
[a] adjusted for maternal and paternal asthma and hay fever, native nationality, parental education, breastfeeding, older siblings, day-care attendance, maternal smoking during pregnancy, parental smoking at home, mould/dampness at home, pets, use of gas for cooking, municipality (BAMSE only), and cohort.

Supplementary Figure 15. Adjusted [a] age-specific odds ratios of the associations of air pollution exposure at the birth address with asthma prevalence excluding data from the PIAMA cohort.



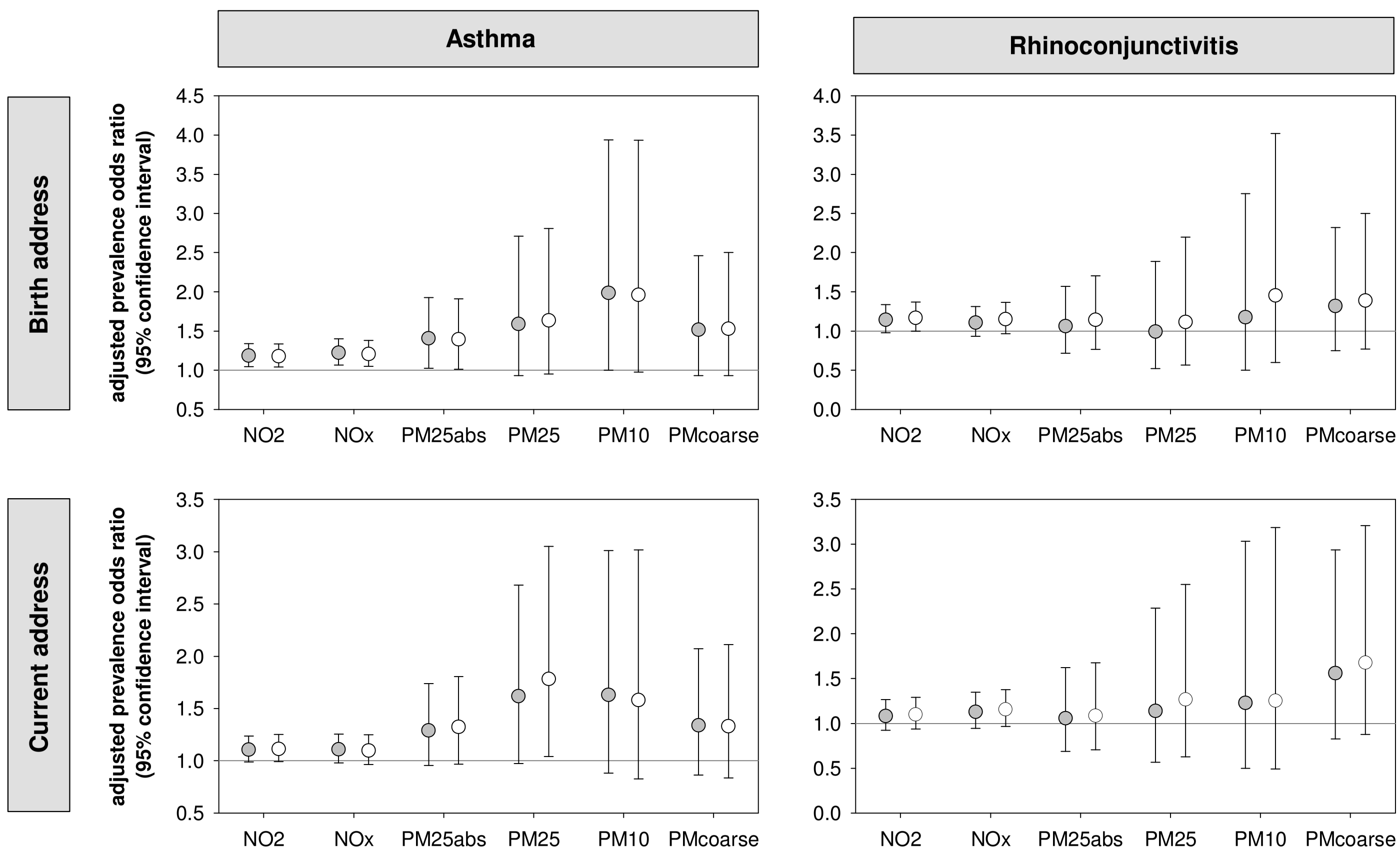
[a] adjusted for maternal and paternal asthma and hay fever, native nationality, parental education, breastfeeding, older siblings, day-care attendance, maternal smoking during pregnancy, parental smoking at home, mould/dampness at home, pets, use of gas for cooking, municipality (BAMSE only), and cohort.

Supplementary Figure 16. Adjusted [a] odds ratios of the associations of air pollution exposure with asthma and rhinoconjunctivitis incidence in PIAMA using data of all follow-ups (grey dots) and data of selected follow-ups (white dots).



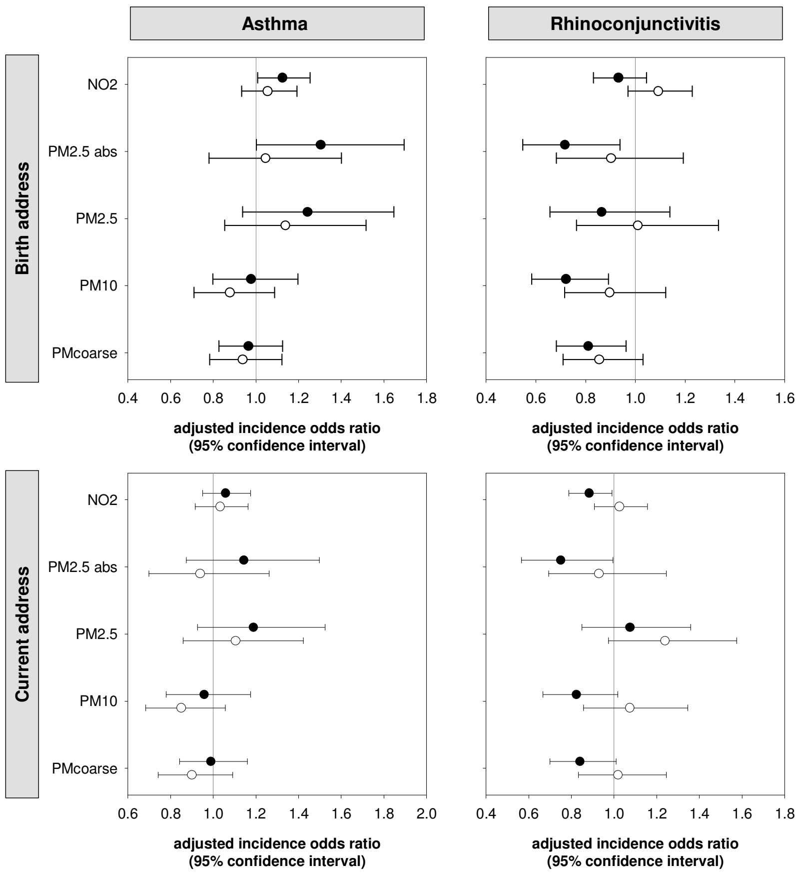
[a] adjusted for maternal and paternal asthma and hay fever, native nationality, parental education, breastfeeding, older siblings, day-care attendance, maternal smoking during pregnancy, parental smoking at home, mould/dampness at home, pets, use of gas for cooking.

Supplementary Figure 17. Adjusted [a] odds ratios of the associations of air pollution exposure with asthma and rhinoconjunctivitis prevalence in PIAMA using data of all follow-ups (grey dots) and data of selected follow-ups (white dots).



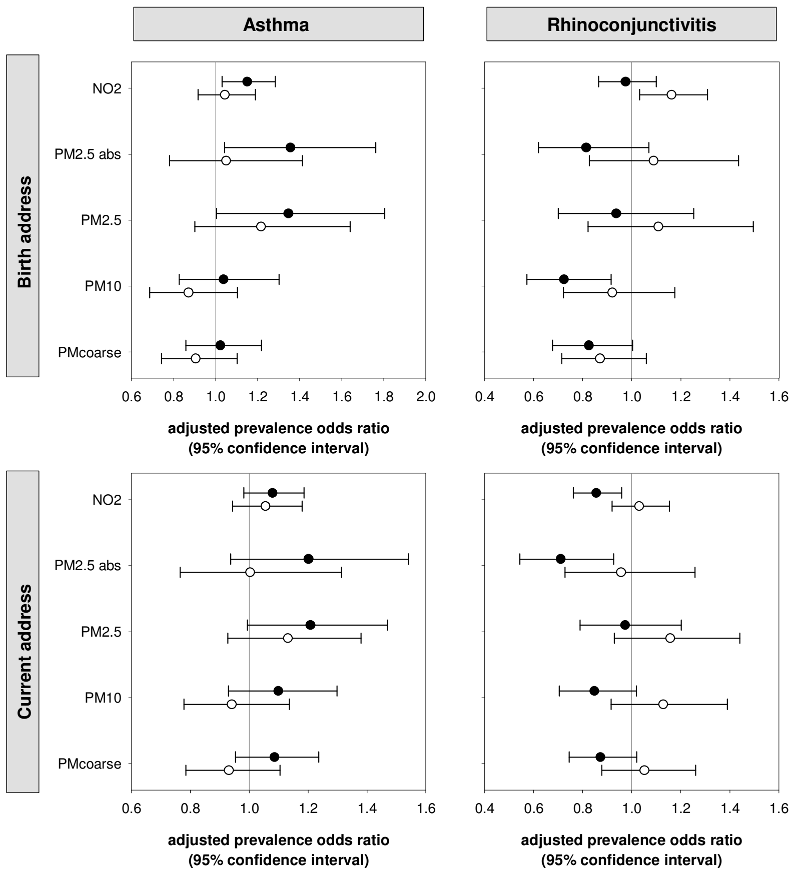
[a] adjusted for maternal and paternal asthma and hay fever, native nationality, parental education, breastfeeding, older siblings, day-care attendance, maternal smoking during pregnancy, parental smoking at home, mould/dampness at home, pets, use of gas for cooking.

Supplementary Figure 18. Adjusted [a] odds ratios of the associations of air pollution exposure at the birth address with asthma and rhinoconjunctivitis incidence by sex from pooled analysis. Black dots represent associations for boys, white dots represent associations for girls.



[a] adjusted for maternal and paternal asthma and hay fever, native nationality, parental education, breastfeeding, older siblings, day-care attendance, maternal smoking during pregnancy, parental smoking at home, mould/dampness at home, pets, use of gas for cooking, municipality (BAMSE only) and cohort.

Supplementary Figure 19. Adjusted [a] odds ratios of the associations of air pollution exposure at the birth address with asthma and rhinoconjunctivitis prevalence by sex from pooled analysis. Black dots represent associations for boys, white dots represent associations for girls.



[a] adjusted for maternal and paternal asthma and hay fever, native nationality, parental education, breastfeeding, older siblings, day-care attendance, maternal smoking during pregnancy, parental smoking at home, mould/dampness at home, pets, use of gas for cooking, municipality (BAMSE only), and cohort.