

Supplemental Materials

Associations of exposure to outdoor PM_{2.5} and NO₂ during pregnancy with childhood asthma, rhinitis, and eczema in a predominantly rural French mother-child cohort.

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Tables

Table S1. Main characteristics of each air pollution model.

Model	Estimation method	Pollutant	Resolution	R ²	Year of monitoring data	Source of monitoring data
Western European Land Use Regression^a	Land Use Regression	PM _{2.5} (µg/m ³)	100×100m	0.62	2010	European Environment Agency (EEA) AirBase v8 dataset
		NO ₂ (µg/m ³)		0.59		
Hybrid model^b	GAM (using spatiotemporal and spatial predictors, and 3 base learners [LMM, GMRF, RF])	PM _{2.5} (µg/m ³)	1km x 1km	0.76	2000 to 2019	Regional air quality monitoring networks (federated by ATMO France)
CHIMERE^c	Eulerian chemistry-transport model	NO ₂ (µg/m ³)	4km x 4km	0.51	2000 to 2015	National air quality databases: – BDQA (Base de Données de Qualité de l’Air) before 2013. – GEODAIR and the Airbase database after 2013.

PM_{2.5} particulate matter with an aerodynamic diameter less than 2.5 µm; NO₂: nitrogen dioxide; LMM: linear mixed models; RF: random forests.

References:

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Table S2. Comparison of baseline characteristics between the analysis populations and the non-respondents to the 6- and 12-year follow-up.

	6-year follow-up			12-year follow-up		
	Non-respondents (n=686)	Analysis population (n=1322)	p-value	Non-respondents (n=888)	Analysis population (n=1118)	p-value
Sex, n (%)			0.73			0.67
Boys	349 (50.9)	662 (50.1)		454 (51.1)	561 (50.2)	
Girls	337 (49.1)	660 (49.9)		434 (48.9)	557 (49.8)	
Mother's age in years at inclusion, mean (SD)*	30.0 (4.35)	30.5 (3.99)	0.007	30.0 (4.32)	30.7 (3.98)	0.0002
Mother tobacco smoking during pregnancy, n (%)			0.02			<.0001
Non-smoker or former smoker	502 (73.7)	1019 (77.1)		633 (71.9)	881 (78.8)	
Smoker at the start of pregnancy who has quit	83 (12.2)	171 (12.9)		114 (13.0)	141 (12.6)	
Smoker at inclusion	96 (14.1)	132 (10.0)		133 (15.1)	96 (8.6)	
Mother's education level at inclusion, n (%)			0.20			<.0001
Under high school	107 (15.7)	188 (14.2)		173 (19.5)	122 (10.9)	
High school diploma	132 (19.3)	223 (16.9)		177 (20.0)	186 (16.6)	
Graduate education	444 (65.0)	911 (68.9)		536 (60.5)	810 (72.5)	
French Deprivation Index (FDep) during pregnancy, n (%)			0.61			0.002
1 st tertile (low deprived)	327 (48.5)	667 (50.5)		402 (45.6)	589 (52.7)	
2 nd tertile (medium deprived)	212 (31.5)	412 (31.1)		286 (32.4)	343 (30.7)	

3 rd tertile (high deprived)	135 (20.0)	243 (18.4)		194 (22.0)	186 (16.6)	
Urbanization degree during pregnancy, <i>n</i> (%)			0.84			0.38
Urban	241 (35.3)	473 (35.8)		309 (34.9)	411 (36.8)	
Rural	441 (64.7)	849 (64.2)		577 (65.1)	707 (63.2)	
Air pollutants concentration ($\mu\text{g}/\text{m}^3$) during pregnancy, <i>median (IQR)</i> †						
PM _{2.5}	15.1 (3.5)	15.1 (3.3)	0.64	14.8 (3.2)	15.3 (3.5)	<.0001
NO ₂	17.3 (9.9)	17.5 (9.6)	0.80	16.9 (9.1)	17.8 (9.9)	0.007

All comparison tests were performed excluding missing data among the non-respondents. *Student's t-test. †Wilcoxon Rank Sum test.

Table S3. Baseline characteristics of participants in 6- and 12-year follow-up according to their area of residence (urban or rural) during pregnancy.

	6-year follow-up (n=1322)			12-year follow-up (n=1118)		
	Urban area (n=473)	Rural area (n=849)	p-value	Urban area (n=411)	Rural area (n=707)	p-value
Sex, n (%)			0.56			0.47
Boys	242 (51.2)	420 (49.5)		212 (51.6)	349 (49.4)	
Girls	231 (48.8)	429 (50.5)		199 (48.4)	358 (50.6)	
Child's age in years, mean (SD)*	6.2 (0.21)	6.2 (0.20)	0.11	12.6 (0.34)	12.6 (0.34)	0.35
Mother's age in years at inclusion, mean (SD)*	30.9 (4.16)	30.3 (3.89)	0.02	30.9 (4.11)	30.6 (3.89)	0.22
Mother tobacco smoking during pregnancy, n (%)			0.28			
Non-smoker or former smoker	354 (74.8)	665 (78.3)		319 (77.6)	562 (79.5)	0.63
Smoker at the start of pregnancy who has quit	70 (14.8)	101 (11.9)		57 (13.9)	84 (11.9)	
Smoker at inclusion	49 (10.4)	83 (9.8)		35 (8.5)	61 (8.6)	
Mother's education level at inclusion, n (%)			0.02			0.006
Under high school	56 (11.8)	132 (15.5)		31 (7.6)	91 (12.9)	
High school diploma	68 (14.4)	155 (18.3)		61 (14.8)	125 (17.7)	
Graduate education	349 (73.8)	562 (66.2)		319 (77.6)	491 (69.4)	
French Deprivation Index (FDep) during pregnancy, n (%)			<.0001			<.0001
1 st tertile (low deprived)	335 (70.8)	332 (39.1)		309 (75.2)	280 (39.6)	

2 nd tertile (medium deprived)	85 (18.0)	327 (38.5)		68 (16.5)	275 (38.9)	
3 rd tertile (high deprived)	53 (11.2)	190 (22.4)		34 (8.3)	152 (21.5)	
Air pollutants concentration ($\mu\text{g}/\text{m}^3$) during pregnancy, mean (median; IQR) †						
PM _{2.5}	16.1 (16.3; 3.2)	14.6 (14.5; 3.2)	<.0001	16.2 (16.5; 3.3)	14.7 (14.8; 3.3)	<.0001
NO ₂	25.3 (24.0; 10.8)	15.1 (14.4; 6.8)	<.0001	26.0 (24.7; 11.5)	15.3 (14.7; 6.9)	<.0001
Outcomes' prevalence						
Ever asthma	59 (12.5)	98 (11.5)	0.62	51 (12.4)	61 (8.6)	0.04
Ever rhinitis	84 (17.8)	175 (20.6)	0.21	94 (22.9)	165 (23.3)	0.86
Ever eczema	117 (24.7)	178 (20.9)	0.11	79 (19.2)	133 (18.8)	0.87
Multimorbidity phenotype			0.82			0.44
1 disease	132 (27.9)	225 (26.5)		101 (24.6)	190 (26.9)	
≥ 2 diseases	56 (11.8)	98 (11.5)		52 (12.7)	74 (10.5)	

*Means were compared using Student's t-test. †Means were compared using Wilcoxon Rank Sum test.

Table S4. Baseline characteristics of participants according to their status for ever asthma, ever rhinitis, and ever eczema at 6-year follow-up.

	Total (n=1322)	Ever asthma			Ever rhinitis			Ever eczema		
		No	Yes	p-value	No	Yes	p-value	No	Yes	p-value
Sex, n (%)				0.02			0.09			0.01
Boys	662 (50.1)	570 (48.9)	92 (58.6)		520 (48.9)	142 (54.8)		495 (48.2)	167 (56.6)	
Girls	660 (49.9)	595 (51.1)	65 (41.4)		543 (51.1)	117 (45.2)		532 (51.8)	128 (43.4)	
Child's age in years, mean (SD)*	6.2 (0.20)	6.2 (0.19)	6.2 (0.23)	0.24	6.2 (0.20)	6.2 (0.19)	0.93	6.2 (0.20)	6.2 (0.18)	0.11
Mother tobacco smoking during pregnancy, n (%)				0.40			0.44			0.21
Non-smoker or former smoker	1019 (77.1)	904 (77.6)	115 (73.3)		826 (77.7)	193 (74.5)		801 (78.0)	218 (73.9)	
Smoker at the start of pregnancy who has quit	171 (12.9)	149 (12.8)	22 (14.0)		136 (12.8)	35 (13.5)		131 (12.8)	40 (13.6)	
Smoker at inclusion	132 (10.0)	112 (9.6)	20 (12.7)		101 (9.5)	31 (12.0)		95 (9.2)	37 (12.5)	
Mother's age at inclusion in years, mean (SD)*	30.5 (3.99)	30.6 (3.9)	29.9 (3.9)	0.04	30.7 (4.0)	29.8 (3.8)	0.001	30.6 (4.0)	30.2 (3.8)	0.22
Mother's education level at inclusion, n (%)				0.37			0.07			0.98
Under high school	188 (14.2)	162 (13.9)	26 (16.6)		154 (14.5)	34 (13.1)		145 (14.1)	43 (14.6)	
High school diploma	223 (16.9)	202 (17.3)	21 (13.4)		167 (15.7)	56 (21.6)		174 (16.9)	49 (16.6)	
Graduate education	991 (68.9)	801 (68.8)	110 (70.0)		742 (69.8)	169 (65.3)		708 (69.0)	203 (68.8)	
French Deprivation Index (FDep) during pregnancy, n (%)				0.22			0.06			0.85
1 st tertile (low deprived)	667 (50.4)	588 (50.5)	79 (50.3)		550 (51.8)	117 (45.2)		515 (50.2)	152 (51.5)	
2 nd tertile (medium deprived)	412 (31.2)	356 (30.5)	56 (35.7)		330 (31.0)	82 (31.6)		324 (31.5)	88 (29.8)	
3 rd tertile (high deprived)	243 (18.4)	221 (19.0)	22 (14.0)		183 (17.2)	60 (23.2)		188 (18.3)	55 (18.7)	
Urbanization degree during pregnancy, n (%)				0.62			0.21			0.11
Urban	473 (35.8)	414 (35.5)	59 (37.6)		389 (36.6)	84 (32.4)		356 (34.7)	117 (39.7)	

Rural	849 (64.2)	751 (64.5)	98 (62.4)		674 (63.4)	175 (67.6)		671 (65.3)	178 (60.3)	
Air pollutants concentration ($\mu\text{g}/\text{m}^3$) during pregnancy, mean (SD)[†]										
PM _{2.5}	15.1 (2.2)	15.1 (2.2)	15.2 (2.2)	0.80	15.1 (2.2)	15.2 (2.2)	0.77	15.1 (2.2)	15.1 (2.3)	0.96
NO ₂	18.8 (7.7)	18.7 (7.7)	19.0 (8.4)	0.99	18.8 (7.7)	18.6 (7.8)	0.47	18.6 (7.5)	19.4 (8.5)	0.32

PM_{2.5} particulate matter with an aerodynamic diameter less than 2.5 μm ; NO₂: nitrogen dioxide; SD: standard deviation. *Means were compared using Student's t-test. †Means were compared using Wilcoxon Rank Sum test.

Table S5. Baseline characteristics of participants according to their status for ever asthma, ever rhinitis, and ever eczema at 12-year follow-up.

	Total (n=1118)	Ever asthma			Ever rhinitis			Ever eczema		
		No	Yes	p-value	No	Yes	p-value	No	Yes	p-value
Sex, n (%)				0.002			0.0001			0.95
Boys	561 (50.2)	489 (48.6)	72 (64.3)		404 (47.0)	157 (60.6)		455 (50.2)	106 (50.0)	
Girls	557 (49.8)	517 (51.4)	40 (35.7)		455 (53.0)	102 (39.4)		451 (49.8)	106 (50.0)	
Child's age in years, mean (SD) *	12.6 (0.33)	12.6 (0.33)	12.6 (0.31)	0.56	12.6 (0.33)	12.6 (0.34)	0.60	12.6 (0.33)	12.6 (0.33)	0.67
Mother tobacco smoking during pregnancy, n (%)				0.06			0.29			0.43
Non-smoker or former smoker	881 (78.8)	802 (79.7)	79 (70.5)		679 (79.1)	202 (78.0)		718 (79.2)	163 (76.9)	
Smoker at the start of pregnancy who has quit	141 (12.6)	123 (12.2)	18 (16.1)		112 (13.0)	29 (11.2)		115 (12.7)	26 (12.3)	
Smoker at inclusion	96 (8.6)	81 (8.1)	15 (13.4)		68 (7.9)	28 (10.8)		73 (8.1)	23 (10.8)	
Mother's age at inclusion in years, mean (SD) *	30.7 (3.97)	30.7 (3.94)	30.4 (4.27)	0.49	30.8 (3.88)	30.4 (4.24)	0.18	30.7 (3.98)	30.7 (3.91)	0.94
Mother's education level at inclusion, n (%)				0.47			0.22			0.03
Under high school	122 (10.9)	106 (10.5)	16 (14.3)		88 (10.2)	34 (13.1)		105 (11.6)	17 (8.0)	
High school diploma	186 (16.6)	169 (16.8)	17 (15.2)		150 (17.5)	36 (13.9)		160 (17.7)	26 (12.3)	
Graduate education	810 (72.5)	731 (72.7)	79 (70.5)		621 (72.3)	189 (73.0)		641 (70.7)	169 (79.7)	
French Deprivation Index (FDep) during pregnancy, n (%)				0.52			0.70			0.22
1 st tertile (low deprived)	589 (52.7)	525 (52.2)	64 (57.1)		449 (52.3)	140 (54.0)		466 (51.4)	123 (58.0)	
2 nd tertile (medium deprived)	343 (30.7)	310 (30.8)	33 (29.5)		269 (31.3)	74 (28.6)		286 (31.6)	57 (26.9)	
3 rd tertile (high deprived)	186 (16.6)	171 (17.0)	15 (13.4)		141 (16.4)	45 (17.4)		154 (17.0)	32 (15.1)	
Urbanization degree during pregnancy, n (%)				0.04			0.86			0.87
Urban	411 (36.8)	360 (35.8)	51 (45.5)		317 (36.9)	94 (36.3)		332 (36.6)	79 (37.3)	

Rural	707 (63.2)	646 (64.2)	61 (54.5)		542 (63.1)	165 (63.7)		574 (63.4)	133 (62.7)	
Air pollutants concentration ($\mu\text{g}/\text{m}^3$) during pregnancy, mean (SD)[†]										
PM _{2.5}	15.3 (2.2)	15.2 (2.2)	15.7 (2.2)	0.03	15.3 (2.2)	15.2 (2.2)	0.54	15.2 (2.2)	15.4 (2.2)	0.45
NO ₂	19.2 (8.0)	19.0 (7.8)	20.9 (9.4)	0.05	19.2 (7.9)	19.2 (8.3)	0.84	19.1 (7.9)	19.7 (8.4)	0.42

PM_{2.5} particulate matter with an aerodynamic diameter less than 2.5 μm ; NO₂: nitrogen dioxide; SD: standard deviation. *Means were compared using Student's t-test. †Means were compared using Wilcoxon Rank Sum test.

Table S6. Baseline characteristics of participants according to the categories of the multimorbidity phenotype at 6- and 12-year follow-ups.

	6-year follow-up					12-year follow-up				
	Total (n=1322)	No disease	1 disease	≥ 2 diseases	p-value	Total (n=1118)	No disease	1 disease	≥ 2 diseases	p-value
Sex, n (%)					0.02					0.007
Boys	662 (50.1)	383 (47.2)	191 (53.5)	88 (57.1)		561 (50.2)	333 (47.5)	149 (51.2)	79 (62.7)	
Girls	660 (49.9)	428 (52.8)	166 (46.5)	66 (42.9)		557 (49.8)	368 (52.5)	142 (48.8)	47 (37.3)	
Child's age in years, mean (SD)	6.2 (0.20)	6.2 (0.20)	6.17 (0.17)	6.22 (0.22)	0.04	12.6 (0.33)	12.6 (0.33)	12.6 (0.35)	12.6 (0.31)	0.92
Mother tobacco smoking during pregnancy, n (%)					0.07					0.35
Non-smoker or former smoker	1019 (77.1)	638 (78.7)	268 (75.1)	113 (73.4)		881 (78.8)	557 (79.5)	231 (79.4)	93 (73.8)	
Smoker at the start of pregnancy who has quit	171 (12.9)	99 (12.2)	55 (15.4)	17 (11.0)		141 (12.6)	91 (13.0)	33 (11.3)	17 (13.5)	
Smoker at inclusion	132 (10.0)	74 (9.1)	34 (9.5)	24 (15.6)		96 (8.6)	53 (7.5)	27 (9.3)	16 (12.7)	
Mother's age at inclusion in years, mean (SD)	30.5 (3.99)	30.8 (4.07)	30.4 (3.84)	29.6 (3.81)	0.005	30.7 (3.97)	30.7 (3.93)	30.7 (3.96)	30.2 (4.23)	0.45
Mother's education level at inclusion, n (%)					0.69					0.25
Under high school	188 (14.2)	116 (14.3)	51 (14.3)	21 (13.6)		122 (10.9)	70 (10.0)	39 (13.4)	13 (10.3)	
High school diploma	223 (16.9)	136 (17.8)	55 (15.4)	32 (20.8)		186 (16.6)	128 (18.3)	40 (13.8)	18 (14.3)	
Graduate education	991 (68.9)	559 (68.9)	251 (70.3)	101 (65.6)		810 (72.5)	503 (71.7)	212 (72.8)	95 (75.4)	
French Deprivation Index (FDep) during pregnancy, n (%)					0.04					0.41
1 st tertile (low deprived)	667 (50.4)	411 (50.7)	185 (51.8)	71 (46.1)		589 (52.7)	356 (50.8)	166 (57.0)	67 (53.2)	
2 nd tertile (medium deprived)	412 (31.2)	261 (32.2)	93 (26.1)	58 (37.7)		343 (30.7)	227 (32.4)	77 (26.5)	39 (30.9)	
3 rd tertile (high deprived)	243 (18.4)	139 (17.1)	58 (22.1)	25 (16.2)		186 (16.6)	118 (16.8)	48 (16.5)	20 (15.9)	

Urbanization degree during pregnancy, <i>n</i> (%)					0.82					0.44
Urban	473 (35.8)	285 (35.1)	132 (37.0)	56 (36.4)		411 (36.8)	258 (36.8)	101 (34.7)	52 (41.3)	
Rural	849 (64.2)	526 (64.9)	225 (63.0)	98 (63.6)		707 (63.2)	443 (63.2)	190 (65.3)	74 (58.7)	
Air pollutants concentration ($\mu\text{g}/\text{m}^3$) during pregnancy, <i>mean</i> (<i>SD</i>)										
PM _{2.5}	15.1 (2.2)	15.1 (2.2)	15.2 (2.2)	15.1 (2.3)	0.56	15.3 (2.2)	15.3 (2.7)	15.2 (2.2)	15.6 (2.3)	0.19
NO ₂	18.8 (7.7)	18.4 (7.3)	19.5 (8.6)	18.7 (7.9)	0.41	19.2 (8.0)	19.1 (8.0)	18.8 (7.4)	20.8 (9.6)	0.26

PM_{2.5} particulate matter with an aerodynamic diameter less than 2.5 μm ; NO₂: nitrogen dioxide; SD: standard deviation.

Table S7. Descriptive statistics of PM_{2.5} and NO₂ exposure during pregnancy among participants at 6- and 12-year follow-ups. Comparative of estimates from the Western European Land Use Regression (LUR) with the estimates from the hybrid and CHIMERE models for continental France.

Pollutant	Model	Mean	SD	Min	25th	50th	75th	Max	IQR
6-years follow-up respondents									
PM _{2.5} µg/m ³	Western European LUR	15.13	2.20	8.34	13.47	15.14	16.79	20.97	3.32
	Hybrid model	10.17	0.77	8.41	9.62	10.08	10.57	13.42	0.95
NO ₂ µg/m ³	Western European LUR	18.75	7.74	5.11	12.91	17.51	22.47	57.06	9.56
	CHIMERE	16.35	3.04	10.58	14.06	16.10	18.02	26.46	3.95
12-years follow-up respondents									
PM _{2.5} µg/m ³	Western European LUR	15.28	2.24	8.34	13.57	15.28	17.10	20.97	3.53
	Hybrid model	10.23	0.80	8.47	9.67	10.13	10.63	13.90	0.95
NO ₂ µg/m ³	Western European LUR	19.22	8.04	5.11	13.22	17.77	23.14	69.23	9.92
	CHIMERE	16.57	3.16	10.58	14.19	16.22	18.40	26.47	4.21

PM_{2.5} particulate matter with an aerodynamic diameter less than 2.5 µm; NO₂: nitrogen dioxide; SD: standard deviation; IQR: interquartile range.

Table S8. Results from univariate and multivariate logistic regression models investigating the associations of exposure to PM_{2.5} during pregnancy with ever asthma, ever rhinitis, ever eczema, and multimorbidity phenotype at 6- and 12-year follow-ups.

Disease	Univariate			Model 1			Model 2			Model 3		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
6-year follow-up												
Ever asthma	1.03	[0.80-1.32]	0.82	1.02	[0.79-1.32]	0.85	1.02	[0.79-1.31]	0.91	1.01	[0.77-1.32]	0.94
Ever rhinitis	1.04	[0.85-1.28]	0.71	1.05	[0.85-1.29]	0.67	1.06	[0.86-1.30]	0.60	1.11	[0.90-1.38]	0.33
Ever eczema	0.99	[0.81-1.20]	0.89	1.01	[0.83-1.23]	0.90	1.01	[0.83-1.23]	0.92	0.99	[0.80-1.22]	0.93
Multimorbidity phenotype												
No disease	Ref.			Ref.			Ref.			Ref.		
1 disease	1.12	[0.92-1.35]	0.26	1.14	[0.95-1.38]	0.17	1.14	[0.94-1.38]	0.19	1.14	[0.93-1.38]	0.21
≥ 2 diseases	1.00	[0.77-1.29]	0.97	1.00	[0.77-1.31]	0.99	1.01	[0.77-1.31]	0.96	1.03	[0.79-1.36]	0.82
12-year follow-up												
Ever asthma	1.41	[1.03-1.93]	0.03	1.42	[1.03-1.96]	0.03	1.42	[1.03-1.96]	0.03	1.38	[0.98-1.93]	0.07
Ever rhinitis	0.93	[0.75-1.16]	0.52	0.95	[0.76-1.18]	0.62	0.93	[0.75-1.17]	0.55	0.91	[0.72-1.15]	0.43
Ever eczema	1.10	[0.87-1.40]	0.41	1.12	[0.88-1.42]	0.37	1.08	[0.85-1.37]	0.54	1.03	[0.80-1.33]	0.83
Multimorbidity phenotype												
No disease	Ref.			Ref.			Ref.			Ref.		
1 disease	0.94	[0.76-1.17]	0.60	0.95	[0.76-1.18]	0.60	0.93	[0.75-1.17]	0.54	0.87	[0.69-1.10]	0.25

≥ 2 diseases	1.25	[0.92-1.69]	0.15	1.29	[0.94-1.76]	0.11	1.26	[0.92-1.72]	0.14	1.26	[0.90-1.74]	0.17
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PM_{2.5} particulate matter with an aerodynamic diameter less than 2.5 μm; OR: Odds Ratio; CI: confidence interval. OR (95% CI) were calculated for an increase of an interquartile range in PM_{2.5} (3.32 μg/m³ for participants at 6-years follow-up, and 3.53 μg/m³ for participants at 12-years follow-up).

Multivariate models were performed with an increasing order of adjustment: **model 1**: adjusted by child's sex and age, mother's age at birth, and mother's smoking habits during pregnancy, **model 2**: adjustment model 1 + mother's education level at birth, and **model 3**: adjustment model 2 + area-level socioeconomic status during pregnancy (French Deprivation Index).

Table S9. Results from univariate and multivariate logistic regression models investigating the associations of exposure to NO₂ during pregnancy with ever asthma, ever rhinitis, ever eczema, and the multimorbidity phenotype at 6- and 12-year follow-ups.

Disease	Univariate			Model 1			Model 2			Model 3		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
6-year follow-up												
Ever asthma	1.05	[0.86-1.28]	0.65	1.04	[0.85-1.27]	0.71	1.03	[0.84-1.26]	0.77	1.03	[0.83-1.28]	0.81
Ever rhinitis	0.96	[0.81-1.14]	0.65	0.96	[0.81-1.14]	0.64	0.97	[0.82-1.15]	0.71	1.01	[0.85-1.21]	0.89
Ever eczema	1.14	[0.98-1.33]	0.10	1.16	[0.99-1.35]	0.07	1.15	[0.99-1.35]	0.07	1.15	[0.97-1.36]	0.10
Multimorbidity phenotype												
No disease	Ref.			Ref.			Ref.			Ref.		
1 disease	1.18	[1.02-1.37]	0.03	1.20	[1.03-1.39]	0.02	1.19	[1.02-1.39]	0.02	1.20	[1.02-1.41]	0.03
≥ 2 diseases	1.04	[0.84-1.29]	0.73	1.04	[0.84-1.29]	0.72	1.04	[0.84-1.30]	0.70	1.08	[0.86-1.35]	0.52
12-year follow-up												
Ever asthma	1.30	[1.04-1.62]	0.02	1.27	[1.02-1.59]	0.04	1.28	[1.02-1.60]	0.03	1.25	[0.98-1.59]	0.07
Ever rhinitis	1.01	[0.85-1.19]	0.96	1.00	[0.84-1.18]	0.98	1.00	[0.84-1.18]	0.96	0.98	[0.81-1.18]	0.80
Ever eczema	1.10	[0.92-1.32]	0.29	1.10	[0.92-1.32]	0.28	1.07	[0.89-1.29]	0.45	1.03	[0.85-1.25]	0.79
Multimorbidity phenotype												
No disease	Ref.			Ref.			Ref.			Ref.		
1 disease	0.95	[0.80-1.13]	0.54	0.95	[0.80-1.13]	0.53	0.94	[0.79-1.13]	0.52	0.88	[0.73-1.07]	0.19

≥ 2 diseases	1.26	[1.01-1.56]	0.04	1.24	[1.00-1.54]	0.05	1.22	[0.98-1.52]	0.07	1.23	[0.97-1.56]	0.09
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NO₂: nitrogen dioxide; OR: Odds Ratio; CI: confidence interval. OR (95% CI) were calculated for an increase of an interquartile range in NO₂ (9.56 µg/m³ for participants at 6-years follow-up, and 9.92 µg/m³ for participants at 12-years follow-up).

Multivariate models were performed with an increasing order of adjustment: *model 1*: adjusted by child's sex and age, mother's age at birth, and mother's smoking habits during pregnancy, *model 2*: adjustment model 1 + mother's education level at birth, and *model 3*: adjustment model 2 + area-level socioeconomic status during pregnancy (French Deprivation Index).

Table S10. Interaction p-value for the degree of urbanization during pregnancy and child's sex with pregnancy exposure to PM_{2.5} and NO₂ among included participants for the 6- and 12-year follow-up analyses

Outcome	Urbanization during pregnancy		Child's sex	
	PM _{2.5} p-value	NO ₂ p-value	PM _{2.5} p-value	NO ₂ p-value
6-year follow-up				
Ever asthma	0.58	0.53	0.86	0.72
Ever rhinitis	0.45	0.39	0.52	0.67
Ever eczema	0.05	0.10	0.30	0.64
Multimorbidity	0.63	0.64	0.97	0.77
12-year follow-up				
Ever asthma	0.23	0.64	0.73	0.30
Ever rhinitis	0.81	0.76	0.64	0.16
Ever eczema	0.58	0.53	0.53	0.15
Multimorbidity	0.43	0.75	0.93	0.19

Table S11. Sex-stratified adjusted associations of pregnancy exposure to PM_{2.5} and NO₂ with ever asthma, ever rhinitis, ever eczema, and the multimorbidity phenotype at 6- and 12-year follow-ups.

Disease	PM _{2.5}						NO ₂					
	Boys			Girls			Boys			Girls		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
6-year follow-up												
Ever asthma	1.08	[0.75-1.54]	0.68	0.98	[0.66-1.47]	0.94	1.03	[0.77-1.37]	0.85	1.07	[0.76-1.51]	0.65
Ever rhinitis	1.23	[0.90-1.67]	0.19	1.01	[0.73-1.38]	0.98	1.00	[0.78-1.28]	0.99	1.03	[0.79-1.35]	0.83
Ever eczema	0.90	[0.68-1.20]	0.48	1.12	[0.83-1.52]	0.46	1.12	[0.90-1.40]	0.32	1.21	[0.94-1.55]	0.14
Multimorbidity phenotype												
No disease	Ref.			Ref.			Ref.			Ref.		
1 disease	1.21	[0.91-1.61]	0.19	1.09	[0.82-1.44]	0.57	1.28	[1.03-1.60]	0.03	1.15	[0.91-1.46]	0.25
≥ 2 diseases	1.04	[0.71-1.52]	0.84	1.05	[0.70-1.57]	0.83	1.03	[0.75-1.41]	0.84	1.15	[0.81-1.62]	0.43
12-year follow-up												
Ever asthma	1.28	[0.83-1.97]	0.27	1.49	[0.85-2.60]	0.17	1.24	[0.93-1.66]	0.14	1.21	[0.77-1.90]	0.41
Ever rhinitis	0.82	[0.60-1.13]	0.22	0.98	[0.68-1.41]	0.89	1.07	[0.85-1.35]	0.57	0.80	[0.58-1.09]	0.16
Ever eczema	1.03	[0.71-1.48]	0.88	1.00	[0.69-1.43]	0.98	1.12	[0.87-1.46]	0.38	0.88	[0.65-1.19]	0.42
Multimorbidity phenotype												
No disease	Ref.			Ref.			Ref.			Ref.		

1 disease	0.80	[0.57-1.12]	0.19	0.94	[0.68-1.31]	0.71	1.00	[0.77-1.29]	0.97	0.76	[0.57-1.01]	0.06
≥ 2 diseases	1.14	[0.74-1.74]	0.55	1.30	[0.77-2.20]	0.32	1.31	[0.98-1.76]	0.07	1.03	[0.67-1.57]	0.91

PM_{2.5} particulate matter with an aerodynamic diameter less than 2.5 µm; NO₂: nitrogen dioxide; OR: Odds Ratio; CI: confidence interval.

OR (95% CI) were calculated for an increase of an interquartile range (3.32 µg/m³ for PM_{2.5}, and 9.56 µg/m³ for NO₂ for participants at 6-years follow-up, and 3.53µg/m³ for PM_{2.5}, and 9.92 µg/m³ for NO₂ for participants at 12-years follow-up). All models were adjusted for child's age, mother's age and education level at birth, mother's tobacco smoking habits during pregnancy and area-level socioeconomic status during pregnancy (French Deprivation Index).

Table S12. Adjusted associations of pregnancy exposure to PM_{2.5} and NO₂ categorized into quartiles with ever asthma, ever rhinitis, and ever eczema at 6- and 12-year follow-ups.

	Ever asthma				Ever rhinitis				Ever eczema			
	OR	95% CI	p-value	p-for-trend	OR	95% CI	p-value	p-for-trend	OR	95% CI	p-value	p-for-trend
PM_{2.5}												
6-year follow-up												
1 st quartile	Ref.			0.79				0.30				0.98
2 nd quartile	1.00	[0.61-1.64]	0.99		0.98	[0.66-1.46]	0.94		0.96	[0.66-1.40]	0.84	
3 rd quartile	1.38	[0.86-2.22]	0.18		1.17	[0.79-1.74]	0.43		1.01	[0.69-1.46]	0.97	
4 th quartile	0.95	[0.57-1.59]	0.85		1.18	[0.79-1.77]	0.42		0.99	[0.67-1.45]	0.95	
12-year follow-up												
1 st quartile	Ref.			0.10				0.50				0.99
2 nd quartile	1.56	[0.83-2.90]	0.17		1.12	[0.75-1.66]	0.59		1.22	[0.79-1.88]	0.36	
3 rd quartile	1.95	[1.05-3.62]	0.04		1.09	[0.72-1.64]	0.69		0.95	[0.60-1.50]	0.84	
4 th quartile	1.71	[0.90-3.25]	0.11		0.86	[0.56-1.33]	0.50		1.09	[0.69-1.72]	0.71	
NO₂												
6-year follow-up												
1 st quartile	Ref.			0.68				0.78				0.27
2 nd quartile	0.93	[0.58-1.50]	0.77		1.02	[0.69-1.49]	0.94		0.95	[0.65-1.38]	0.79	

3 rd quartile	0.81	[0.49-1.32]	0.39		0.87	[0.58-1.29]	0.48		0.75	[0.50-1.11]	0.14	
4 th quartile	0.94	[0.57-1.54]	0.80		0.99	[0.66-1.49]	0.97		1.34	[0.92-1.95]	0.13	
12-year follow-up												
1 st quartile	Ref.											
2 nd quartile	1.73	[0.93-3.20]	0.08	0.17	1.13	[0.76-1.69]	0.55	0.71	0.93	[0.60-1.43]	0.72	0.80
3 rd quartile	1.83	[0.98-3.42]	0.06		1.03	[0.68-1.56]	0.89		0.86	[0.55-1.35]	0.51	
4 th quartile	1.65	[0.86-3.15]	0.13		0.95	[0.61-1.46]	0.80		0.96	[0.61-1.50]	0.85	

PM_{2.5} particulate matter with an aerodynamic diameter less than 2.5 µm; NO₂: nitrogen dioxide; OR: Odds Ratio; CI: confidence interval.

All models were adjusted for child's sex and age, mother's age and education level at birth, mother's tobacco smoking habits during pregnancy and area-level socioeconomic status during pregnancy (French Deprivation Index).

Table S13. Adjusted associations of ever asthma, ever rhinitis, ever eczema, and the multimorbidity phenotype among children at 6- and 12-year follow-ups with PM_{2.5} and NO₂ pregnancy exposure estimates from the hybrid and CHIMERE models for continental France.

Disease	PM _{2.5} (Hybrid model)			NO ₂ (CHIMERE model)		
	OR	95% CI	p-value	OR	95% CI	p-value
6-year follow-up						
Ever asthma	0.98	[0.79-1.21]	0.85	1.04	[0.83-1.31]	0.74
Ever rhinitis	1.01	[0.85-1.20]	0.93	0.99	[0.82-1.20]	0.92
Ever eczema	1.15	[0.98-1.35]	0.10	1.14	[0.96-1.37]	0.14
Multimorbidity phenotype						
No disease	Ref.			Ref.		
1 disease	1.14	[0.93-1.38]	0.21	1.20	[1.02-1.41]	0.03
≥ 2 diseases	1.03	[0.79-1.36]	0.82	1.08	[0.86-1.35]	0.52
12-year follow-up						
Ever asthma	1.29	[1.03-1.63]	0.03	1.30	[0.99-1.69]	0.06
Ever rhinitis	0.91	[0.76-1.09]	0.30	0.94	[0.77-1.16]	0.57
Ever eczema	1.05	[0.87-1.26]	0.62	1.02	[0.82-1.26]	0.87
Multimorbidity phenotype						
No disease	Ref.			Ref.		
1 disease	0.87	[0.69-1.10]	0.25	0.88	[0.73-1.07]	0.19

≥ 2 diseases	1.26	[0.90-1.74]	0.17	1.23	[0.97-1.56]	0.09
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PM_{2.5} particulate matter with an aerodynamic diameter less than 2.5 µm; NO₂: nitrogen dioxide; OR: Odds Ratio; CI: confidence interval.

OR (95% CI) were calculated for an increase of an interquartile range (0.95 µg/m³ for PM_{2.5}, and 3.95 µg/m³ for NO₂ for participants at 6-years follow-up, and 0.95 µg/m³ for PM_{2.5}, and 4.21 µg/m³ for NO₂ for participants at 12-years follow-up). All models were adjusted for child's age, mother's age and education level at birth, mother's tobacco smoking habits during pregnancy and area-level socioeconomic status during pregnancy (French Deprivation Index).

Table S14. Comparison of Adjusted Odds Ratios (OR) and Relative Risks (RR) for pregnancy exposure to PM_{2.5} and NO₂. Associations with ever asthma, ever rhinitis, and ever eczema, at 6- and 12-year follow-ups using logistic regression models, and Poisson regression models with robust error variance.

Disease	PM _{2.5}						NO ₂					
	Logistic regression			Poisson regression with robust error variance			Logistic regression			Poisson regression with robust error variance		
	OR	95% CI	p-value	RR	95% CI	p-value	OR	95% CI	p-value	RR	95% CI	p-value
6-year follow-up (n = 1322)												
Ever asthma	1.01	[0.77-1.32]	0.94	1.01	[0.79-1.29]	0.94	1.03	[0.83-1.28]	0.81	1.02	[0.84-1.25]	0.82
Ever rhinitis	1.11	[0.90-1.38]	0.33	1.09	[0.90-1.32]	0.39	1.01	[0.85-1.21]	0.89	1.01	[0.86-1.19]	0.90
Ever eczema	0.99	[0.80-1.22]	0.93	0.99	[0.83-1.19]	0.94	1.15	[0.97-1.36]	0.10	1.11	[0.96-1.28]	0.15
12-year follow-up (n = 1118)												
Ever asthma	1.38	[0.98-1.93]	0.07	1.33	[0.96-1.83]	0.08	1.25	[0.98-1.59]	0.07	1.21	[0.97-1.50]	0.09
Ever rhinitis	0.91	[0.72-1.15]	0.43	0.93	[0.76-1.14]	0.50	0.98	[0.81-1.18]	0.80	0.98	[0.84-1.15]	0.83
Ever eczema	1.03	[0.80-1.33]	0.83	1.02	[0.82-1.28]	0.85	1.03	[0.85-1.25]	0.79	1.02	[0.86-1.21]	0.81

PM_{2.5} particulate matter with an aerodynamic diameter less than 2.5 µm; NO₂: nitrogen dioxide; OR: Odds Ratio; CI: confidence interval; RR: Relative Risk.

OR and RR (95% CI) were calculated for an increase of an interquartile range (3.32 µg/m³ for PM_{2.5}, and 9.56 µg/m³ for NO₂ for participants at 6-years follow-up, and 3.53 µg/m³ for PM_{2.5}, and 9.92 µg/m³ for NO₂ for participants at 12-years follow-up). All models were adjusted for child's sex and age, mother's age and education level at birth, mother's tobacco smoking habits during pregnancy and area-level socioeconomic status during pregnancy (French Deprivation Index).

Table S15. Comparison of Adjusted Odds Ratios (OR) and Relative Risks (RR) for pregnancy exposure to PM_{2.5} and NO₂. Associations with ever asthma, ever rhinitis, and ever eczema, at 6- and 12-year follow-ups using logistic regression models, and log-binomial regression models.

Disease	PM _{2.5}						NO ₂					
	Logistic regression			Log-binomial regression			Logistic regression			Log-binomial regression		
	OR	95% CI	p-value	RR	95% CI	p-value	OR	95% CI	p-value	RR	95% CI	p-value
6-year follow-up (n = 1322)												
Ever asthma	1.01	[0.77-1.32]	0.94	1.01	[0.80-1.27]	0.96	1.03	[0.83-1.28]	0.81	1.03	[0.85-1.24]	0.78
Ever rhinitis	1.11	[0.90-1.38]	0.33	1.09	[0.92-1.29]	0.34	1.01	[0.85-1.21]	0.89	1.01	[0.88-1.16]	0.90
Ever eczema	0.99	[0.80-1.22]	0.93	0.99	[0.84-1.16]	0.89	1.15	[0.97-1.36]	0.10	1.11	[0.98-1.26]	0.09
12-year follow-up (n = 1118)												
Ever asthma	1.38	[0.98-1.93]	0.07	1.32	[0.97-1.78]	0.07	1.25	[0.98-1.59]	0.07	1.23	[0.99-1.51]	0.06
Ever rhinitis	0.91	[0.72-1.15]	0.43	0.94	[0.79-1.12]	0.48	0.98	[0.81-1.18]	0.80	0.99	[0.86-1.15]	0.94
Ever eczema	1.03	[0.80-1.33]	0.83	1.02	[0.83-1.25]	0.85	1.03	[0.85-1.25]	0.79	1.02	[0.87-1.18]	0.84

PM_{2.5} particulate matter with an aerodynamic diameter less than 2.5 µm; NO₂: nitrogen dioxide; OR: Odds Ratio; CI: confidence interval; RR: Relative Risk.

OR and RR (95% CI) were calculated for an increase of an interquartile range (3.32 µg/m³ for PM_{2.5}, and 9.56 µg/m³ for NO₂ for participants at 6-years follow-up, and 3.53µg/m³ for PM_{2.5}, and 9.92 µg/m³ for NO₂ for participants at 12-years follow-up). All models were adjusted for child's sex and age, mother's age and education level at birth, mother's tobacco smoking habits during pregnancy and area-level socioeconomic status during pregnancy (French Deprivation Index).

Figures

Figure S1. Participants' department of residence during pregnancy.

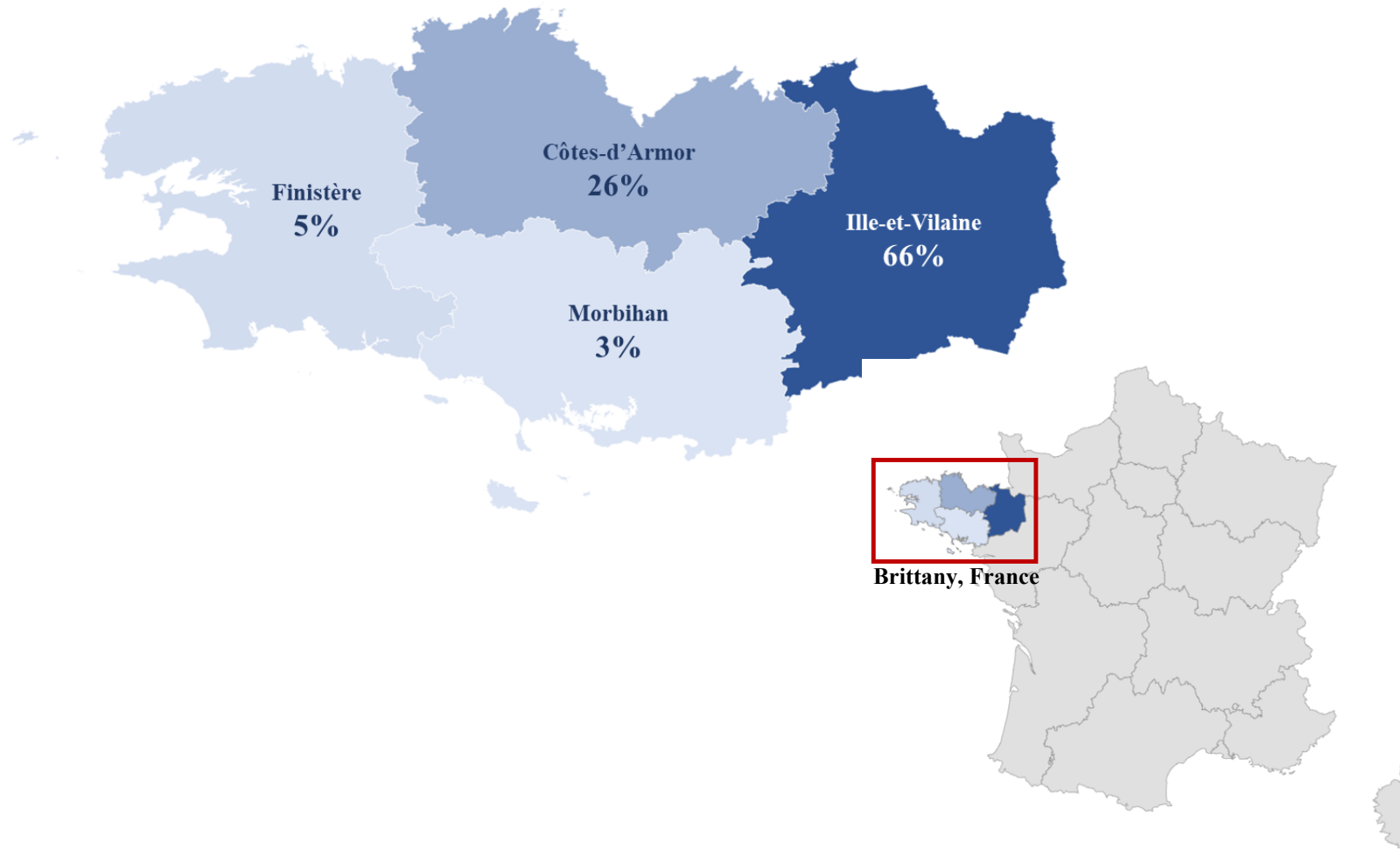
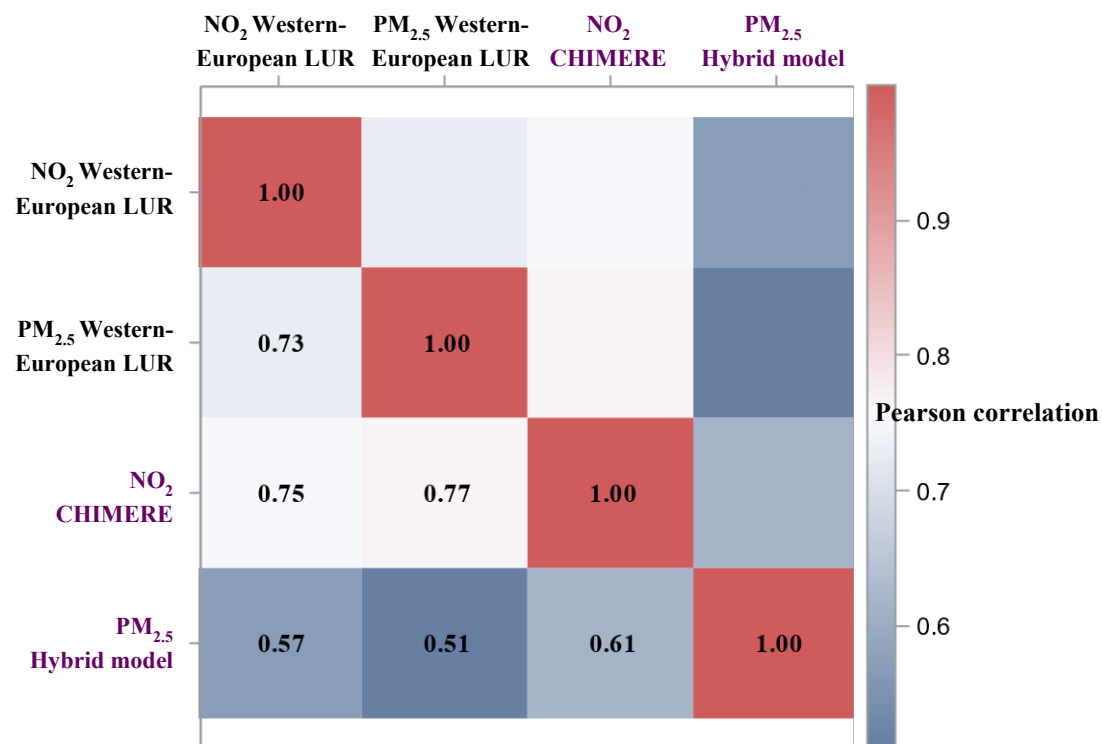


Figure S2. Correlation coefficients between PM_{2.5} and NO₂ estimates from the Western-European LUR, the hybrid, and the CHIMERE models.



All coefficients have a p-value <0.0001

PM_{2.5} particulate matter with an aerodynamic diameter less than 2.5 μm; NO₂: nitrogen dioxide.

Figure S3. Relationship PM_{2.5} and ever doctor-diagnosed asthma, ever rhinitis, and ever doctor-diagnosed eczema at 6-year follow-up. Comparison of fully adjusted logistic regression models with and without restricted cubic splines.

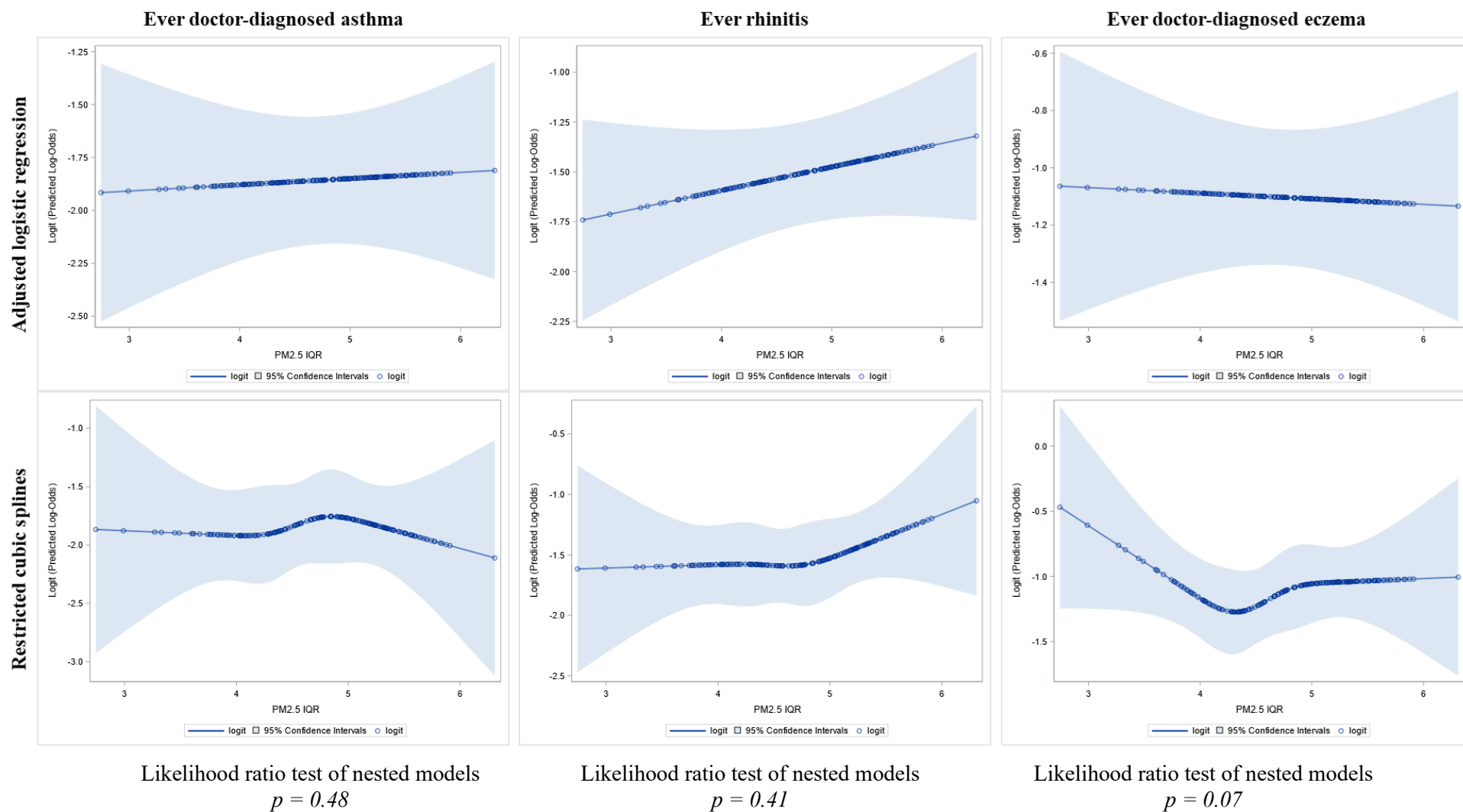


Figure S4. Relationship NO₂ and ever doctor-diagnosed asthma, ever rhinitis, and ever doctor-diagnosed eczema at 6-year follow-up. Comparison of fully adjusted logistic regression models with and without restricted cubic splines.

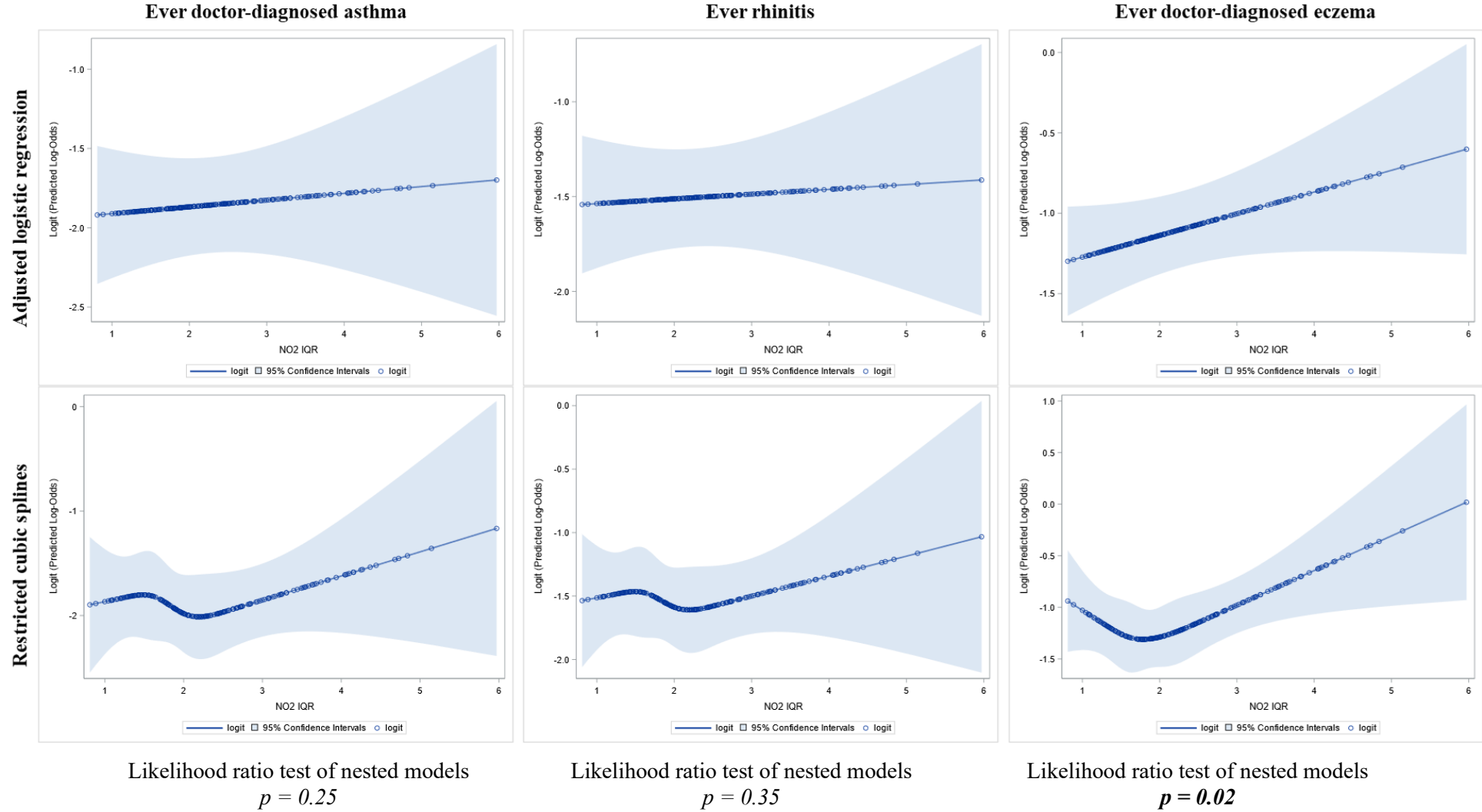


Figure S5. Relationship PM_{2.5} and ever doctor-diagnosed asthma, ever rhinitis, and ever doctor-diagnosed eczema at 12-year follow-up. Comparison of fully adjusted logistic regression models with and without restricted cubic splines.

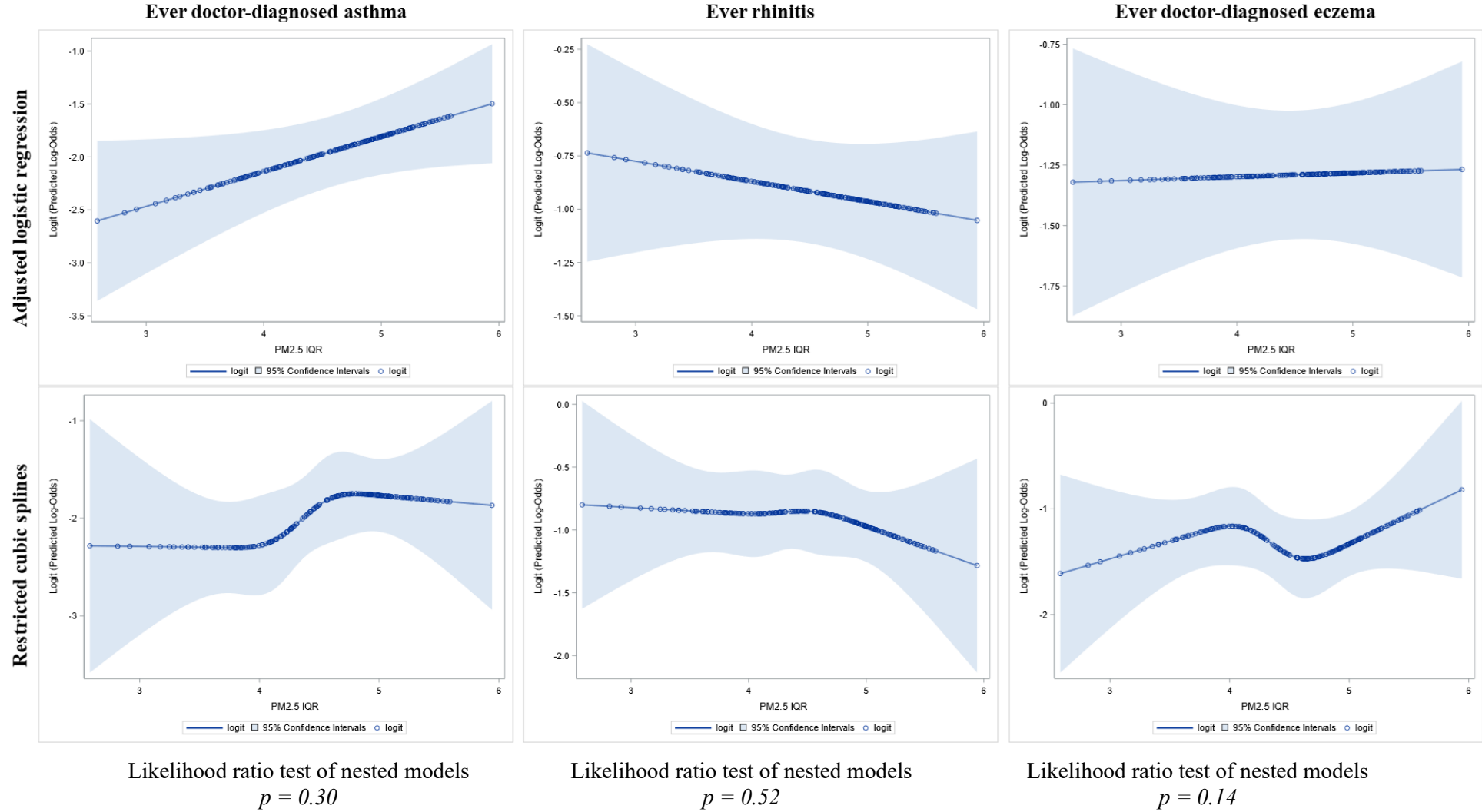


Figure S6. Relationship NO₂ and ever doctor-diagnosed asthma, ever rhinitis, and ever doctor-diagnosed eczema at 12-year follow-up. Comparison of fully adjusted logistic regression models with and without restricted cubic splines.

