

Supplemental Materials

Effects of urban and rural surrounding residential greenness during pregnancy on childhood asthma, rhinitis, eczema, and their comorbidity: findings from the French mother-child cohort Pélégie.

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Tables

Table S1. Comparison of baseline characteristics between respondents and non-respondents to 6- and 12-year follow-up among the 3322 singleton live births eligible for follow-up.

	Singleton live births eligible for follow-up (n=3322)					
	6-year follow-up			12-year follow-up		
	Respondents (n=1418)	Non-respondents (n=1904)	p-value	Respondents (n=1211)	Non-respondents (n=2111)	p-value
Sex, n (%)			0.84			0.79
Boys	710 (50.1)	960 (50.4)		605 (50.0)	1065 (50.5)	
Girls	708 (49.9)	944 (49.6)		606 (50.0)	1046 (49.5)	
Mother's age in years at inclusion, mean (SD)*	30.58 (4.02)	29.72 (4.43)	<0.0001	30.70 (3.98)	29.73 (4.41)	<0.0001
Mother tobacco smoking during pregnancy, n (%)			<0.0001			<0.0001
Non-smoker or former smoker	1087 (77.3)	1273 (67.6)		953 (79.2)	1407 (67.5)	
Smoker at the start of pregnancy who has quit	182 (12.9)	285 (15.2)		150 (12.5)	317 (15.2)	
Smoker at inclusion	138 (9.8)	323 (17.2)		100 (8.3)	361 (17.3)	
Mother's education level at inclusion, n (%)			<0.0001			<0.0001
Under high school	199 (14.1)	426 (22.4)		130 (10.8)	495 (23.5)	
High school diploma	243 (17.2)	380 (20.1)		198 (16.4)	425 (20.2)	
Graduate education	974 (68.7)	1092 (57.5)		880 (72.8)	1186 (56.3)	

French Deprivation Index (FDep) during pregnancy, n (%)			0.59			0.004
1 st tertile (low deprived)	712 (50.7)	925 (49.5)		635 (53.2)	1002 (48.1)	
2 nd tertile (medium deprived)	438 (31.2)	579 (31.0)		362 (30.4)	655 (31.5)	
3 rd tertile (high deprived)	255 (18.1)	365 (19.5)		195 (16.4)	425 (20.4)	
Season at the start of pregnancy, n (%)			0.59			0.63
Spring	346 (24.4)	463 (24.3)		307 (25.4)	502 (23.8)	
Summer	370 (26.1)	536 (28.2)		325 (26.8)	581 (27.5)	
Autumn	340 (24.0)	440 (23.1)		289 (23.9)	491 (23.3)	
Winter	362 (25.5)	465 (24.4)		290 (23.9)	537 (25.4)	
Degree of urbanization during pregnancy, n (%)			<0.0001			0.0002
Urban	502 (35.5)	828 (43.7)		434 (36.0)	896 (42.6)	
Rural	914 (64.5)	1065 (56.3)		773 (64.0)	1206 (57.4)	
NDVI during pregnancy, median (IQR)						
100m buffer	0.51 (0.13)	0.48 (0.14)	<0.0001	0.51 (0.13)	0.49 (0.15)	<0.0001
300m buffer	0.54 (0.12)	0.51 (0.13)	<0.0001	0.53 (0.12)	0.51 (0.13)	<0.0001
500m buffer	0.55 (0.11)	0.53 (0.13)	<0.0001	0.55 (0.11)	0.53 (0.12)	<0.0001
Air pollution concentration ($\mu\text{g}/\text{m}^3$) during pregnancy, median (IQR) [†]						
PM _{2.5}	15.15 (3.30)	15.61 (3.72)	<0.0001	15.33 (3.52)	15.45 (3.64)	0.26

Table S2. Baseline characteristics of participants according to their status for ever asthma, ever rhinitis, and ever eczema at 6-year follow-up.

	Total (n=1325)	Ever asthma			Ever rhinitis			Ever eczema		
		No	Yes	p-value	No	Yes	p-value	No	Yes	p-value
Sex, n (%)				0.03			0.09			0.01
Boys	663 (50.0)	571 (48.9)	92 (58.2)		521 (48.9)	142 (54.8)		495 (48.1)	168 (56.8)	
Girls	662 (50.0)	596 (51.1)	66 (41.8)		545 (51.1)	117 (45.2)		534 (51.9)	128 (43.2)	
Child's age in years, mean (SD)	6.20 (0.20)	6.20 (0.20)	6.22 (0.23)	0.46	6.20 (0.21)	6.20 (0.20)	0.58	6.21 (0.21)	6.18 (0.19)	0.14
Mother's age at inclusion in years, mean (SD)	30.54 (3.99)	30.62 (3.99)	29.93 (3.98)	0.03	30.71 (4.01)	29.81 (3.84)	0.001	30.61 (4.04)	30.27 (3.83)	0.31
Mother tobacco smoking during pregnancy, n (%)				0.41			0.43			0.22
Non-smoker or former smoker	1022 (77.1)	906 (77.6)	116 (73.4)		829 (77.7)	193 (74.5)		803 (78.0)	219 (74.0)	
Smoker at the start of pregnancy who has quit	171 (12.9)	149 (12.8)	22 (13.9)		136 (12.8)	35 (13.5)		131 (12.7)	40 (13.5)	
Smoker at inclusion	132 (10.0)	112 (9.6)	20 (12.7)		101 (9.5)	31 (12.0)		95 (9.3)	37 (12.5)	
Mother's education level at inclusion, n (%)				0.36			0.07			0.98
Under high school	188 (14.2)	162 (13.9)	26 (16.5)		154 (14.4)	34 (13.1)		145 (14.1)	43 (14.5)	
High school diploma	223 (16.8)	202 (17.3)	21 (13.3)		167 (15.7)	56 (21.6)		174 (16.9)	49 (16.6)	
Graduate education	914 (69.0)	803 (68.8)	111 (70.2)		745 (69.9)	169 (65.3)		710 (69.0)	204 (68.9)	
French Deprivation Index (FDep) during pregnancy, n (%)				0.19			0.06			0.82
1 st tertile (low deprived)	667 (50.4)	588 (50.4)	79 (50.0)		550 (51.6)	117 (45.2)		515 (50.0)	152 (51.4)	
2 nd tertile (medium deprived)	414 (31.2)	357 (30.6)	57 (36.1)		332 (31.1)	82 (31.6)		326 (31.7)	88 (29.7)	

3 rd tertile (high deprived)	244 (18.4)	222 (19.0)	22 (13.9)		184 (17.3)	60 (23.2)		188 (18.3)	56 (18.9)	
Season at the start of pregnancy, <i>n</i> (%)				0.97			0.58			0.89
Spring	323 (24.4)	283 (24.3)	40 (25.3)		261 (24.5)	62 (23.9)		249 (24.2)	74 (25.0)	
Summer	345 (26.0)	306 (26.2)	39 (24.7)		271 (25.4)	74 (28.6)		273 (26.5)	72 (24.3)	
Autumn	317 (23.9)	278 (23.8)	39 (24.7)		253 (23.7)	64 (24.7)		246 (23.9)	71 (24.0)	
Winter	340 (25.7)	300 (25.7)	40 (25.3)		281 (26.4)	59 (22.8)		261 (25.4)	79 (26.7)	
Degree of urbanization during pregnancy, <i>n</i> (%)				0.65			0.22			0.12
Urban	473 (35.7)	414 (35.5)	59 (37.3)		389 (36.5)	84 (32.4)		356 (34.6)	117 (39.5)	
Rural	852 (64.3)	753 (64.5)	99 (62.7)		677 (63.5)	175 (67.6)		673 (65.4)	179 (60.5)	
NDVI during pregnancy, median (IQR)										
100m buffer	0.51 (0.13)	0.51 (0.14)	0.50 (0.13)	0.27	0.51 (0.13)	0.51 (0.14)	0.91	0.52 (0.13)	0.50 (0.14)	0.03
300m buffer	0.54 (0.12)	0.54 (0.12)	0.53 (0.12)	0.45	0.54 (0.12)	0.54 (0.11)	0.97	0.54 (0.12)	0.54 (0.14)	0.12
500m buffer	0.55 (0.11)	0.55 (0.11)	0.54 (0.12)	0.48	0.55 (0.11)	0.55 (0.11)	0.63	0.55 (0.10)	0.55 (0.13)	0.14
Air pollution concentration ($\mu\text{g}/\text{m}^3$) during pregnancy, median (IQR)										
PM _{2.5}	15.15 (3.32)	15.10 (3.39)	15.23 (3.02)	0.73	15.12 (3.33)	15.23 (3.45)	0.76	15.14 (3.32)	15.18 (3.37)	0.95
Department of residence at inclusion, <i>n</i> (%)										
22 - Côtes-d'Armor	350 (26.4)	314 (26.9)	36 (22.8)		278 (26.1)	72 (27.8)		265 (25.8)	85 (28.7)	
29 - Finistère	75 (5.7)	69 (5.9)	6 (3.8)		60 (5.6)	15 (5.8)		63 (6.1)	12 (4.1)	
35 - Ille-et-Vilaine	861 (65.0)	750 (64.3)	111 (70.3)		696 (65.3)	165 (63.7)		670 (65.1)	191 (64.5)	

56 - Morbihan	39 (2.9)	34 (2.9)	5 (3.2)		32 (3.0)	7 (2.7)		31 (3.0)	8 (2.7)	
Outcomes' prevalence										
Ever asthma, <i>n</i> (%)	158 (11.9)				79 (7.4)	79 (30.5)	<0.0001	88 (8.6)	70 (23.6)	<0.0001
Ever rhinitis, <i>n</i> (%)	259 (19.5)	180 (15.4)	79 (50.0)	<0.0001				162 (15.7)	97 (32.8)	<0.0001
Ever eczema, <i>n</i> (%)	296 (22.3)	226 (19.4)	70 (44.3)	<0.0001	199 (18.7)	97 (37.5)	<0.0001			

NDVI: Normalized Difference Vegetation Index; PM_{2.5}: particulate matter with an aerodynamic diameter less than 2.5 µm; SD: standard deviation.

Table S3. Baseline characteristics of participants according to their status for ever asthma, ever rhinitis, and ever eczema at 12-year follow-up.

	Total (n=1119)	Ever asthma			Ever rhinitis			Ever eczema		
		No	Yes	p-value	No	Yes	p-value	No	Yes	p-value
Sex, n (%)				0.001			0.0001			0.94
Boys	562 (50.2)	589 (48.6)	73 (64.6)		404 (47.0)	158 (60.8)		456 (50.3)	106 (50.0)	
Girls	557 (49.8)	517 (51.4)	40 (35.4)		455 (53.0)	102 (39.2)		451 (49.7)	106 (50.0)	
Child's age in years, mean (SD)	12.61 (0.34)	12.61 (0.34)	12.62 (0.32)	0.71	12.61 (0.33)	12.60 (0.35)	0.76	12.61 (0.34)	12.60 (0.33)	0.73
Mother's age at inclusion in years, mean (SD)	30.68 (3.98)	30.70 (3.94)	30.50 (4.33)	0.58	30.76 (3.89)	30.41 (4.27)	0.14	30.68 (4.00)	30.69 (3.92)	0.83
Mother tobacco smoking during pregnancy, n (%)				0.07			0.29			0.42
Non-smoker or former smoker	882 (78.8)	802 (79.7)	80 (70.8)		679 (79.0)	203 (78.1)		719 (79.3)	163 (76.9)	
Smoker at the start of pregnancy who has quit	141 (12.6)	123 (12.2)	18 (15.9)		112 (13.1)	29 (11.1)		115 (12.7)	26 (12.3)	
Smoker at inclusion	96 (8.6)	81 (8.1)	15 (13.3)		68 (7.9)	28 (10.8)		73 (8.0)	23 (10.8)	
Mother's education level at inclusion, n (%)				0.48			0.22			0.03
Under high school	122 (10.9)	106 (10.5)	16 (14.2)		88 (10.2)	34 (13.1)		105 (11.6)	17 (8.0)	
High school diploma	186 (16.6)	169 (16.8)	17 (15.0)		150 (17.5)	36 (13.8)		160 (17.6)	26 (12.3)	
Graduate education	811 (72.5)	731 (72.7)	80 (70.8)		621 (72.3)	190 (73.1)		642 (70.8)	169 (79.7)	
French Deprivation Index (FDep) during pregnancy, n (%)				0.48			0.68			0.23
1 st tertile (low deprived)	590 (52.7)	525 (52.2)	65 (57.5)		449 (52.3)	141 (54.2)		467 (51.5)	123 (58.0)	
2 nd tertile (medium deprived)	343 (30.7)	310 (30.8)	33 (29.2)		269 (31.3)	74 (28.5)		286 (31.5)	57 (26.9)	

3 rd tertile (high deprived)	186 (16.6)	171 (17.0)	15 (13.3)		141 (16.4)	45 (17.3)		154 (17.0)	32 (15.1)	
Season at the start of pregnancy, <i>n</i> (%)				0.78			0.05			0.67
Spring	287 (25.6)	257 (25.5)	30 (26.5)		208 (24.2)	79 (30.4)		228 (25.1)	59 (27.8)	
Summer	300 (26.8)	266 (26.4)	34 (30.1)		227 (26.4)	73 (28.1)		248 (27.3)	52 (24.5)	
Autumn	261 (23.3)	238 (23.7)	23 (20.4)		201 (23.4)	60 (23.1)		208 (22.9)	53 (25.1)	
Winter	271 (24.2)	245 (24.4)	26 (23.0)		223 (26.0)	48 (18.5)		223 (24.7)	48 (22.6)	
Degree of urbanization during pregnancy, <i>n</i> (%)				0.05			0.83			0.86
Urban	411 (36.7)	360 (35.8)	51 (45.1)		317 (36.9)	94 (36.2)		332 (36.6)	79 (37.3)	
Rural	708 (63.3)	646 (64.2)	62 (54.9)		542 (63.1)	166 (63.8)		575 (63.4)	133 (62.7)	
NDVI during pregnancy, median (IQR)										
100m buffer	0.51 (0.13)	0.51 (0.14)	0.51 (0.12)	0.28	0.51 (0.13)	0.51 (0.14)	0.49	0.51 (0.13)	0.50 (0.14)	0.07
300m buffer	0.54 (0.12)	0.54 (0.12)	0.53 (0.14)	0.15	0.53 (0.12)	0.54 (0.11)	0.32	0.54 (0.12)	0.53 (0.12)	0.52
500m buffer	0.55 (0.12)	0.55 (0.11)	0.53 (0.12)	0.11	0.54 (0.12)	0.55 (0.11)	0.18	0.55 (0.11)	0.55 (0.12)	0.70
Air pollution concentration ($\mu\text{g}/\text{m}^3$) during pregnancy, median (IQR)										
PM _{2.5}	15.28 (3.53)	15.23 (3.54)	16.06 (3.14)	0.04	15.32 (3.56)	15.22 (3.21)	0.48	15.28 (3.51)	15.31 (3.73)	0.44
Department of residence at inclusion, <i>n</i> (%)										
22 - Côtes-d'Armor	286 (25.6)	264 (26.2)	22 (19.5)		223 (26.0)	63 (24.2)		230 (25.4)	56 (26.4)	
29 - Finistère	59 (5.3)	52 (5.2)	7 (6.2)		40 (4.7)	19 (7.3)		45 (5.0)	14 (6.6)	
35 - Ille-et-Vilaine	753 (67.3)	669 (66.5)	84 (74.3)		580 (67.5)	173 (66.5)		614 (67.6)	139 (65.6)	

56 - Morbihan	21 (1.9)	21 (2.1)	0 (0)		16 (1.9)	5 (1.9)		18 (2.0)	3 (1.4)	
Outcomes' prevalence										
Ever asthma, <i>n (%)</i>	113 (10.1)				40 (4.7)	73 (28.1)	<0.0001	63 (6.9)	50 (23.6)	<0.0001
Ever rhinitis, <i>n (%)</i>	260 (23.2)	187 (18.6)	73 (64.6)	<0.0001				176 (19.4)	84 (39.6)	<0.0001
Ever eczema, <i>n (%)</i>	212 (18.9)	162 (16.1)	50 (44.2)	<0.0001	128 (14.9)	84 (32.3)	<0.0001			

NDVI: Normalized Difference Vegetation Index; PM_{2.5}: particulate matter with an aerodynamic diameter less than 2.5 µm; SD: standard deviation.

Table S4. 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=1325)			12-year follow-up (n=1119)		
	Urban area (n=473)	Rural area (n=852)	p-value	Urban area (n=411)	Rural area (n=708)	p-value
Sex, n (%)			0.54			0.49
Boys	242 (51.2)	421 (49.4)		212 (51.6)	350 (49.4)	
Girls	231 (48.8)	431 (50.6)		199 (48.4)	358 (50.6)	
Child's age in years, mean (SD)*	6.21 (0.21)	6.19 (0.20)	0.27	12.62 (0.34)	12.60 (0.34)	0.28
Mother's age in years at inclusion, mean (SD)*	30.89 (4.16)	30.34 (3.89)	0.02	30.86 (4.11)	30.58 (3.90)	0.36
Mother tobacco smoking during pregnancy, n (%)			0.26			0.62
Non-smoker or former smoker	354 (74.8)	668 (78.4)		319 (77.6)	563 (79.5)	
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 (9.7)		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 (18.2)		61 (14.8)	125 (17.7)	
Graduate education	349 (73.8)	565 (66.3)		319 (77.6)	492 (69.4)	
French Deprivation Index (FDep) during pregnancy, n (%)			<0.0001			<0.0001
1 st tertile (low deprived)	335 (70.8)	332 (39.0)		309 (75.2)	281 (39.7)	

2 nd tertile (medium deprived)	85 (18.0)	329 (38.6)		68 (16.5)	275 (38.8)	
3 rd tertile (high deprived)	53 (11.2)	191 (22.4)		34 (8.3)	152 (21.5)	
Season at the start of pregnancy, <i>n</i> (%)			0.12			0.001
Spring	114 (24.1)	209 (24.6)		100 (24.3)	187 (26.4)	
Summer	141 (29.8)	204 (23.9)		138 (33.6)	162 (22.9)	
Autumn	105 (22.2)	212 (24.9)		86 (20.9)	175 (24.7)	
Winter	113 (23.9)	227 (26.6)		87 (21.2)	184 (26.0)	
NDVI during pregnancy, median (IQR)						
100m buffer	0.45 (0.12)	0.55 (0.11)	<0.0001	0.44 (0.11)	0.55 (0.11)	<0.0001
300m buffer	0.46 (0.11)	0.57 (0.09)	<0.0001	0.45 (0.12)	0.57 (0.09)	<0.0001
500m buffer	0.47 (0.11)	0.58 (0.08)	<0.0001	0.47 (0.12)	0.58 (0.08)	<0.0001
Air pollution concentration ($\mu\text{g}/\text{m}^3$) during pregnancy, median (IQR) [†]						
PM _{2.5}	16.25 (3.23)	14.50 (3.24)	<0.0001	16.50 (3.26)	14.75 (3.34)	<0.0001
Outcomes' prevalence						
Ever asthma	59 (12.5)	99 (11.6)	0.65	51 (12.4)	62 (8.8)	0.05
Ever rhinitis	84 (17.8)	175 (20.5)	0.12	94 (22.9)	166 (23.4)	0.83
Ever eczema	117 (24.7)	179 (21.0)	0.12	79 (19.2)	133 (18.8)	0.86
Multimorbidity phenotype			0.85			0.48
No disease	285 (60.3)	527 (61.9)		258 (62.7)	443 (62.6)	

1 disease	132 (27.9)	227 (26.6)		101 (24.6)	190 (26.8)	
≥ 2 diseases	56 (11.8)	98 (11.5)		52 (12.7)	75 (10.6)	

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

Table S5. Baseline characteristics of participants according to the categories of the multimorbidity phenotype at 6- and 12-year follow-ups.

	6-years follow-up					12-years follow-up				
	Total (n=1325)	No disease	1 disease	≥ 2 diseases	p-value	Total (n=1119)	No disease	1 disease	≥ 2 diseases	p-value
Sex, n (%)					0.02					0.005
Boys	663 (50.0)	383 (47.2)	192 (53.5)	88 (57.1)		562 (50.2)	333 (47.5)	149 (51.2)	80 (63.0)	
Girls	662 (50.0)	429 (52.8)	167 (46.5)	66 (42.9)		557 (49.8)	368 (52.5)	142 (48.8)	47 (37.0)	
Child's age in years, mean (SD)	6.20 (0.20)	6.21 (0.21)	6.18 (0.18)	6.22 (0.23)	0.04	12.61 (0.34)	12.61 (0.33)	12.61 (0.36)	12.60 (0.32)	0.90
Mother's age at inclusion in years, mean (SD)	30.54 (3.99)	30.77 (4.07)	30.38 (3.84)	29.65 (3.81)	0.004	30.68 (3.98)	30.75 (3.93)	30.67 (3.96)	30.33 (4.29)	0.55
Mother tobacco smoking during pregnancy, n (%)					0.07					0.36
Non-smoker or former smoker	1022 (77.1)	639 (78.7)	270 (75.2)	113 (73.4)		882 (78.8)	557 (79.5)	231 (79.4)	94 (74.0)	
Smoker at the start of pregnancy who has quit	171 (12.9)	99 (12.2)	55 (15.3)	17 (11.0)		141 (12.6)	91 (13.0)	33 (11.3)	17 (13.4)	
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 (12.6)	
Mother's education level at inclusion, n (%)					0.68					0.24
Under high school	188 (14.2)	116 (14.3)	51 (14.2)	21 (13.6)		122 (10.9)	70 (10.0)	39 (13.4)	13 (10.2)	
High school diploma	223 (16.8)	136 (16.7)	55 (15.3)	32 (20.8)		186 (16.6)	128 (18.3)	40 (13.7)	18 (14.2)	
Graduate education	914 (69.0)	560 (69.0)	253 (70.5)	101 (65.6)		811 (72.5)	503 (71.7)	212 (72.9)	96 (75.6)	
French Deprivation Index (FDep) during pregnancy, n (%)					0.04					0.41
1 st tertile (low deprived)	667 (50.4)	411 (50.6)	185 (51.5)	71 (46.1)		590 (52.7)	356 (50.8)	166 (57.0)	68 (53.6)	
2 nd tertile (medium deprived)	414 (31.2)	262 (32.3)	94 (26.2)	58 (37.7)		343 (30.7)	227 (32.4)	77 (26.5)	39 (30.7)	

3 rd tertile (high deprived)	244 (18.4)	139 (17.1)	80 (22.3)	25 (16.2)		186 (16.6)	118 (16.8)	48 (16.5)	20 (15.7)	
Season at the start of pregnancy, <i>n</i> (%)					0.95					0.56
Spring	323 (24.4)	196 (24.1)	86 (24.0)	41 (26.6)		287 (25.6)	173 (24.7)	74 (25.4)	40 (31.5)	
Summer	345 (26.0)	208 (25.6)	100 (27.9)	37 (24.0)		300 (26.8)	189 (27.0)	76 (26.2)	35 (27.6)	
Autumn	317 (23.9)	196 (24.1)	82 (22.8)	39 (25.3)		261 (23.3)	162 (23.1)	69 (23.7)	30 (23.6)	
Winter	340 (25.7)	212 (26.2)	91 (25.3)	37 (24.0)		271 (24.2)	177 (25.2)	72 (24.7)	22 (17.3)	
Degree of urbanization during pregnancy, <i>n</i> (%)					0.85					0.48
Urban	473 (35.7)	285 (35.1)	132 (36.8)	56 (36.4)		411 (36.7)	258 (36.8)	101 (34.7)	52 (40.9)	
Rural	852 (64.3)	527 (64.9)	227 (63.2)	98 (63.6)		708 (63.3)	443 (63.2)	190 (65.3)	75 (59.1)	
NDVI during pregnancy, median (IQR)										
100m buffer	0.51 (0.13)	0.52 (0.14)	0.50 (0.13)	0.51 (0.13)	0.10	0.51 (0.13)	0.51 (0.13)	0.54 (0.13)	0.55 (0.12)	0.55
300m buffer	0.54 (0.12)	0.54 (0.12)	0.53 (0.13)	0.54 (0.12)	0.09	0.54 (0.12)	0.50 (0.13)	0.53 (0.11)	0.55 (0.10)	0.60
500m buffer	0.55 (0.11)	0.55 (0.10)	0.54 (0.12)	0.55 (0.12)	0.14	0.55 (0.12)	0.51 (0.14)	0.53 (0.12)	0.55 (0.13)	0.53
Air pollution concentration ($\mu\text{g}/\text{m}^3$) during pregnancy, median (IQR)										
PM _{2.5}	15.15 (3.32)	15.05 (3.32)	15.16 (3.46)	15.37 (3.22)	0.46	15.28 (3.53)	15.32 (3.58)	15.13 (3.33)	15.76 (3.64)	0.32
Department of residence at inclusion, <i>n</i> (%)										
22 - Côtes-d'Armor	350 (26.4)	215 (26.5)	91 (25.3)	44 (28.6)		286 (25.6)	184 (26.2)	75 (25.8)	27 (21.3)	
29 - Finistère	75 (5.7)	51 (6.3)	18 (5.1)	6 (3.9)		59 (5.3)	34 (4.9)	13 (4.4)	12 (9.4)	
35 - Ille-et-Vilaine	861 (65.0)	520 (64.0)	241 (67.1)	100 (64.9)		753 (67.3)	468 (66.8)	199 (68.4)	86 (67.7)	

56 - Morbihan	39 (2.9)	26 (3.2)	9 (2.5)	4 (2.6)		21 (1.9)	15 (2.1)	4 (1.4)	2 (1.6)	
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NDVI: Normalized Difference Vegetation Index; PM_{2.5}: particulate matter with an aerodynamic diameter less than 2.5 µm; SD: standard deviation.

Table S6. NDVI descriptive statistics among participants included for analyses at 6- and 12-year follow-up.

Buffer size	Mean	SD	Min	25th	50th	75th	Max	IQR
6-year follow-up (n=1325)								
100 m	0.54	0.08	0.28	0.49	0.55	0.60	0.80	0.11
300 m	0.57	0.07	0.31	0.52	0.57	0.62	0.74	0.09
500 m	0.58	0.06	0.34	0.54	0.58	0.62	0.75	0.08
12-year follow-up (n=1119)								
100 m	0.54	0.08	0.28	0.49	0.55	0.60	0.80	0.11
300 m	0.57	0.07	0.31	0.53	0.57	0.61	0.74	0.09
500 m	0.58	0.06	0.34	0.54	0.58	0.62	0.75	0.08

Table S7. NDVI descriptive statistics by urbanicity among participants included for analyses at 6- and 12-year follow-up.

Buffer size	Urbanicity	Mean	SD	Min	25th	50th	75th	Max	IQR
6-years follow-up respondents (n=1325)									
100 m	Urban (n=473)	0.44	0.10	0.11	0.39	0.45	0.51	0.69	0.12
	Rural (n=852)	0.54	0.08	0.28	0.49	0.55	0.60	0.80	0.11
300 m	Urban (n=473)	0.45	0.09	0.14	0.40	0.46	0.51	0.71	0.11
	Rural (n=852)	0.57	0.07	0.31	0.52	0.57	0.62	0.74	0.09
500 m	Urban (n=473)	0.46	0.09	0.18	0.41	0.47	0.52	0.70	0.11
	Rural (n=852)	0.58	0.06	0.34	0.54	0.58	0.62	0.75	0.08
12-years follow-up respondents (n=1119)									
100 m	Urban (n=411)	0.43	0.10	0.13	0.39	0.44	0.50	0.69	0.11
	Rural (n=708)	0.54	0.08	0.28	0.49	0.55	0.60	0.80	0.11
300 m	Urban (n=411)	0.45	0.09	0.14	0.39	0.45	0.51	0.71	0.12
	Rural (n=708)	0.57	0.07	0.31	0.53	0.57	0.61	0.74	0.09
500 m	Urban (n=411)	0.45	0.09	0.19	0.40	0.47	0.52	0.70	0.12
	Rural (n=708)	0.58	0.06	0.34	0.54	0.58	0.62	0.75	0.08

Table S8. Results from multivariate logistic regression models investigating the associations of surrounding residential greenness during pregnancy (NDVI 300m) with ever asthma, ever rhinitis, ever eczema, and the multimorbidity phenotype among children at 6- and 12-years of follow-up.

Disease	Unadjusted			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-years follow-up (n= 1325)												
Ever asthma	0.94	[0.79-1.11]	0.45	0.94	[0.80-1.12]	0.51	0.95	[0.80-1.13]	0.52	0.94	[0.79-1.13]	0.52
Ever rhinitis	1.01	[0.88-1.17]	0.87	1.02	[0.88-1.17]	0.83	1.01	[0.88-1.17]	0.86	0.99	[0.86-1.15]	0.89
Ever eczema	0.87	[0.77-1.00]	0.05	0.87	[0.76-0.99]	0.04	0.87	[0.76-0.99]	0.04	0.87	[0.76-1.00]	0.05
Multimorbidity phenotype												
No disease	Ref.			Ref.			Ref.			Ref.		
1 disease	0.87	[0.76-0.98]	0.03	0.86	[0.76-0.98]	0.03	0.87	[0.76-0.99]	0.03	0.87	[0.76-0.99]	0.03
≥ 2 diseases	0.94	[0.78-1.12]	0.48	0.94	[0.78-1.12]	0.48	0.94	[0.78-1.12]	0.48	0.92	[0.76-1.11]	0.37
12-years follow-up (n= 1119)												
Ever asthma	0.85	[0.71-1.03]	0.10	0.86	[0.72-1.05]	0.13	0.86	[0.71-1.04]	0.11	0.88	[0.72-1.07]	0.20
Ever rhinitis	1.05	[0.91-1.21]	0.49	1.05	[0.91-1.21]	0.51	1.04	[0.91-1.21]	0.55	1.06	[0.92-1.23]	0.43
Ever eczema	0.92	[0.80-1.07]	0.30	0.92	[0.79-1.07]	0.27	0.94	[0.81-1.09]	0.40	0.96	[0.82-1.13]	0.62
Multimorbidity phenotype												
No disease	Ref.			Ref.			Ref.			Ref.		
1 disease	1.02	[0.89-1.17]	0.76	1.02	[0.89-1.17]	0.80	1.01	[0.88-1.17]	0.87	1.05	[0.91-1.21]	0.53
≥ 2 diseases	0.92	[0.76-1.11]	0.38	0.92	[0.76-1.11]	0.39	0.93	[0.77-1.12]	0.43	0.94	[0.77-1.14]	0.52

NDVI 300m: Normalized Difference Vegetation Index at 300-meters circular buffer around residential address; OR: Odds Ratio; CI: confidence interval.

OR (95% CI) were calculated per 0.1-unit increase of NDVI. 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, *model 3*: adjustment model 2 + area-level socioeconomic status during pregnancy (French Deprivation Index).

Table S9. Interaction p-value for the surrounding residential greenness during pregnancy (NDVI 300m) with the degree of urbanization during pregnancy among included participants for the 6- and 12-year follow-up analyses.

Outcome	Degree of urbanization
6-years follow-up	
Ever asthma	0.80
Ever rhinitis	0.39
Ever eczema	0.57
Multimorbidity	0.69
12-years follow-up	
Ever asthma	0.57
Ever rhinitis	0.66
Ever eczema	0.53
Multimorbidity	0.72

Table S10. Adjusted associations of NDVI 300m categorized into tertiles 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
6-years follow-up												
1 st tertile	Ref.			0.39	Ref.			0.44	Ref.			0.15
2 nd tertile	0.81	[0.53-1.22]	0.31		0.99	[0.71-1.39]	0.96		0.80	[0.58-1.10]	0.17	
3 rd tertile	0.84	[0.55-1.27]	0.40		0.87	[0.62-1.23]	0.44		0.79	[0.57-1.09]	0.16	
12-years follow-up												
1 st tertile	Ref.			0.23	Ref.			0.42	Ref.			0.87
2 nd tertile	1.15	[0.72-1.84]	0.57		1.25	[0.88-1.79]	0.21		1.21	[0.83-1.75]	0.32	
3 rd tertile	0.71	[0.42-1.21]	0.21		1.17	[0.81-1.68]	0.41		1.03	[0.70-1.53]	0.87	

NDVI 300m: Normalized Difference Vegetation Index at 300-meters circular buffer around residential address; OR: Odds Ratio; CI: confidence interval.

OR (95% CI) were calculated per 0.1-unit increase of NDVI. Analyses were conducted using *model 3*: adjusted by child's sex and age, mother's age at inclusion, mother's education level at inclusion, mother's smoking habits during pregnancy, area-level socioeconomic status during pregnancy (French Deprivation Index).

Table S11. Adjusted associations of surrounding residential greenness during pregnancy (NDVI 300m) with ever asthma, ever rhinitis, and ever eczema at 6- and 12-year follow-ups. Logistic regression models further adjusting on air pollution, and season at the start of pregnancy.

Disease	6-year follow-up						12-year follow-up					
	Model 4			Model 5			Model 4			Model 5		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
Ever asthma	0.94	[0.78-1.14]	0.52	0.94	[0.79-1.13]	0.52	0.93	[0.75-1.16]	0.51	0.88	[0.72-1.07]	0.20
Ever rhinitis	1.02	[0.87-1.21]	0.77	0.99	[0.85-1.14]	0.86	1.04	[0.88-1.22]	0.66	1.07	[0.92-1.24]	0.40
Ever eczema	0.85	[0.73-0.98]	0.03	0.87	[0.76-1.00]	0.05	0.96	[0.81-1.15]	0.67	0.96	[0.82-1.12]	0.61
Multimorbidity phenotype												
No disease	Ref.			Ref.			Ref.			Ref.		
1 disease	0.88	[0.76-1.02]	0.08	0.87	[0.76-0.99]	0.03	1.01	[0.86-1.19]	0.88	1.05	[0.91-1.21]	0.53
≥ 2 diseases	0.91	[0.74-1.12]	0.38	0.92	[0.76-1.11]	0.37	0.98	[0.79-1.22]	0.88	0.94	[0.77-1.15]	0.54

NDVI 300m: Normalized Difference Vegetation Index at 300-meters circular buffer around residential address; OR: Odds Ratio; CI: confidence interval.

OR (95% CI) were calculated per 0.1-unit increase of NDVI 300m. **Model 4:** adjusted by child's sex and age, mother's age at birth, and mother's smoking habits during pregnancy, mother's education level at birth, area-level socioeconomic status during pregnancy (French Deprivation Index), and outdoor PM_{2,5} concentration during pregnancy. **Model 5:** adjusted by child's sex and age, mother's age at birth, and mother's smoking habits during pregnancy, mother's education level at birth, area-level socioeconomic status during pregnancy (French Deprivation Index), and season at the start of pregnancy.

Table S12. Adjusted associations of surrounding residential greenness during pregnancy (NDVI 100m, 300m, and 500m) with ever asthma, ever rhinitis, and ever eczema at 6- and 12-year follow-ups.

Disease	NDVI 100m			NDVI 300m			NDVI 500m		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
6-years follow-up (n= 1325)									
Ever doctor-diagnosed asthma	0.92	[0.78-1.08]	0.30	0.94	[0.79-1.13]	0.52	0.95	[0.79-1.15]	0.60
Ever rhinitis	1.00	[0.87-1.15]	0.99	0.99	[0.86-1.15]	0.89	1.02	[0.88-1.19]	0.80
Ever doctor-diagnosed eczema	0.86	[0.76-0.98]	0.02	0.87	[0.76-1.00]	0.05	0.87	[0.75-1.00]	0.05
Multimorbidity phenotype									
No disease	Ref.			Ref.			Ref.		
1 disease	0.88	[0.78-0.99]	0.04	0.87	[0.76-0.99]	0.03	0.87	[0.76-1.00]	0.05
≥ 2 diseases	0.90	[0.76-1.07]	0.25	0.92	[0.76-1.11]	0.37	0.93	[0.76-1.13]	0.47
12-years follow-up (n= 1119)									
Ever doctor-diagnosed asthma	0.91	[0.76-1.11]	0.35	0.88	[0.72-1.07]	0.20	0.86	[0.71-1.06]	0.16
Ever rhinitis	1.04	[0.91-1.20]	0.56	1.06	[0.92-1.23]	0.43	1.08	[0.93-1.26]	0.33
Ever doctor-diagnosed eczema	0.89	[0.76-1.03]	0.11	0.96	[0.82-1.13]	0.62	0.97	[0.83-1.14]	0.71
Multimorbidity phenotype									
No disease	Ref.			Ref.			Ref.		
1 disease	0.98	[0.86-1.13]	0.81	1.05	[0.91-1.21]	0.53	1.07	[0.92-1.25]	0.35
≥ 2 diseases	0.92	[0.76-1.10]	0.35	0.94	[0.77-1.14]	0.52	0.94	[0.77-1.15]	0.57

NDVI 100m, 300m, and 500m: Normalized Difference Vegetation Index at 100-, 300-, and 500-meters circular buffer around residential address; OR: Odds Ratio; CI: confidence interval.

OR (95% CI) were calculated per 0.1-unit increase of NDVI. Sensitivity analyses using *model 3*: adjusted by child's sex and age, mother's age at inclusion, mother's education level at inclusion, mother's smoking habits during pregnancy, area-level socioeconomic status during pregnancy (French Deprivation Index).

Table S13. Associations of surrounding residential greenness during pregnancy (NDVI 300m) with ever asthma, ever rhinitis, and ever eczema, at 6- and 12-year follow-ups. Comparison of Adjusted Odds Ratios (OR) from logistic regression models, and Relative Risks (RR) from Poisson regression models with robust error variance and log-binomial regression models.

Disease	Logistic regression			Poisson regression with robust error variance			Log-binomial regression		
	OR	95% CI	p-value	RR	95% CI	p-value	RR	95% CI	p-value
6-year follow-up (n = 1325)									
Ever asthma	0.94	[0.79-1.13]	0.52	0.95	[0.81-1.12]	0.54	0.95	[0.82-1.10]	0.47
Ever rhinitis	0.99	[0.86-1.15]	0.89	0.99	[0.87-1.13]	0.90	0.99	[0.89-1.11]	0.87
Ever eczema	0.87	[0.76-1.00]	0.05	0.90	[0.80-1.02]	0.08	0.90	[0.82-1.00]	0.04
12-year follow-up (n = 1119)									
Ever asthma	0.88	[0.72-1.07]	0.20	0.89	[0.74-1.08]	0.22	0.89	[0.75-1.06]	0.18
Ever rhinitis	1.06	[0.92-1.23]	0.43	1.05	[0.92-1.19]	0.51	1.04	[0.93-1.16]	0.53
Ever eczema	0.96	[0.82-1.13]	0.62	0.97	[0.85-1.12]	0.67	0.97	[0.86-1.10]	0.62

NDVI 300m: Normalized Difference Vegetation Index at 300-meters circular buffer around residential address; OR: Odds Ratio; CI: confidence interval.

OR and RR (95% CI) were calculated per 0.1-unit increase of NDVI 300m. Sensitivity analyses using *model 3*: adjusted by child's sex and age, mother's age at inclusion, mother's education level at inclusion, mother's smoking habits during pregnancy, area-level socioeconomic status during pregnancy (French Deprivation Index).

Figures

Figure S1. Department of residence during pregnancy of participants included for analyses.

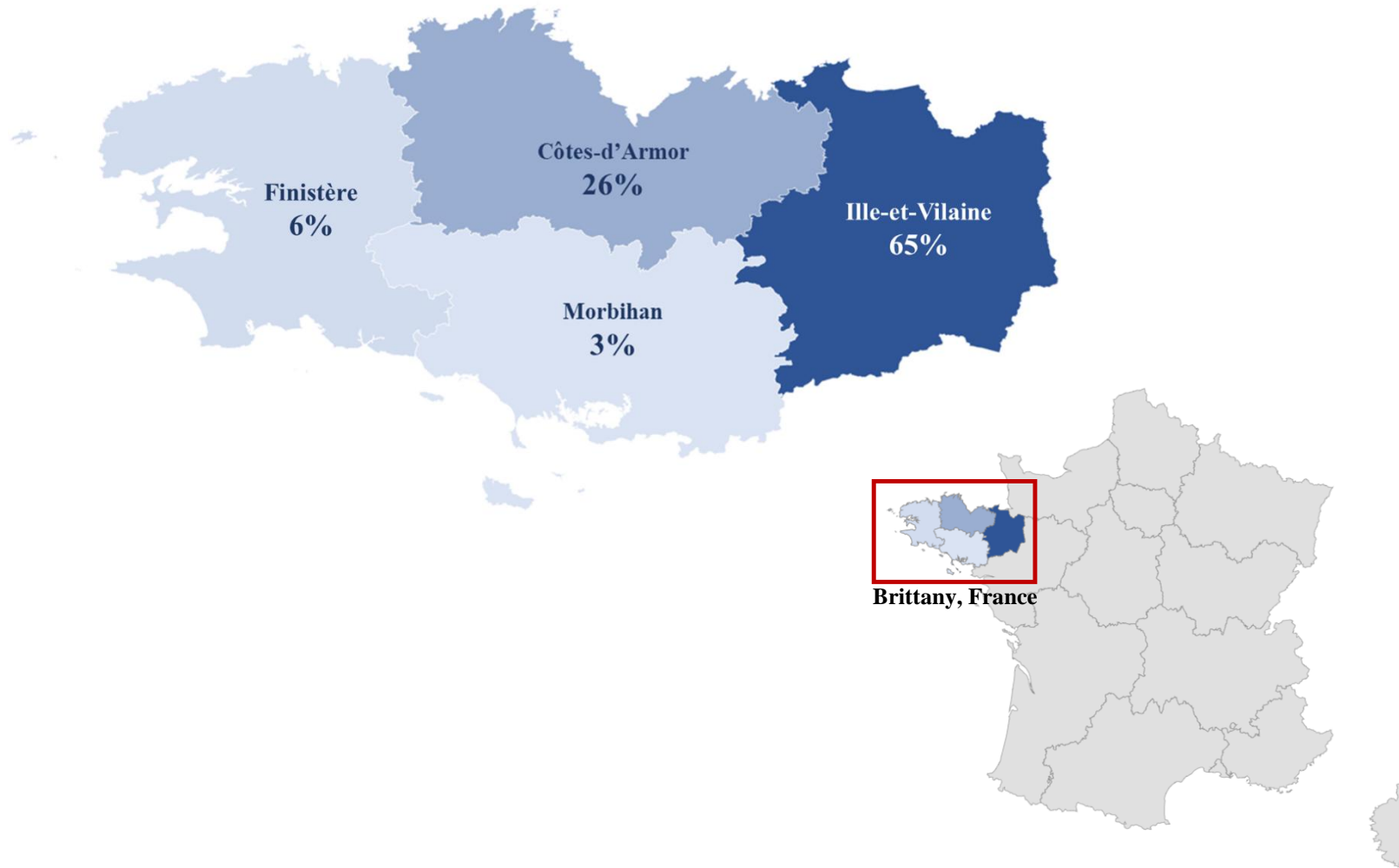
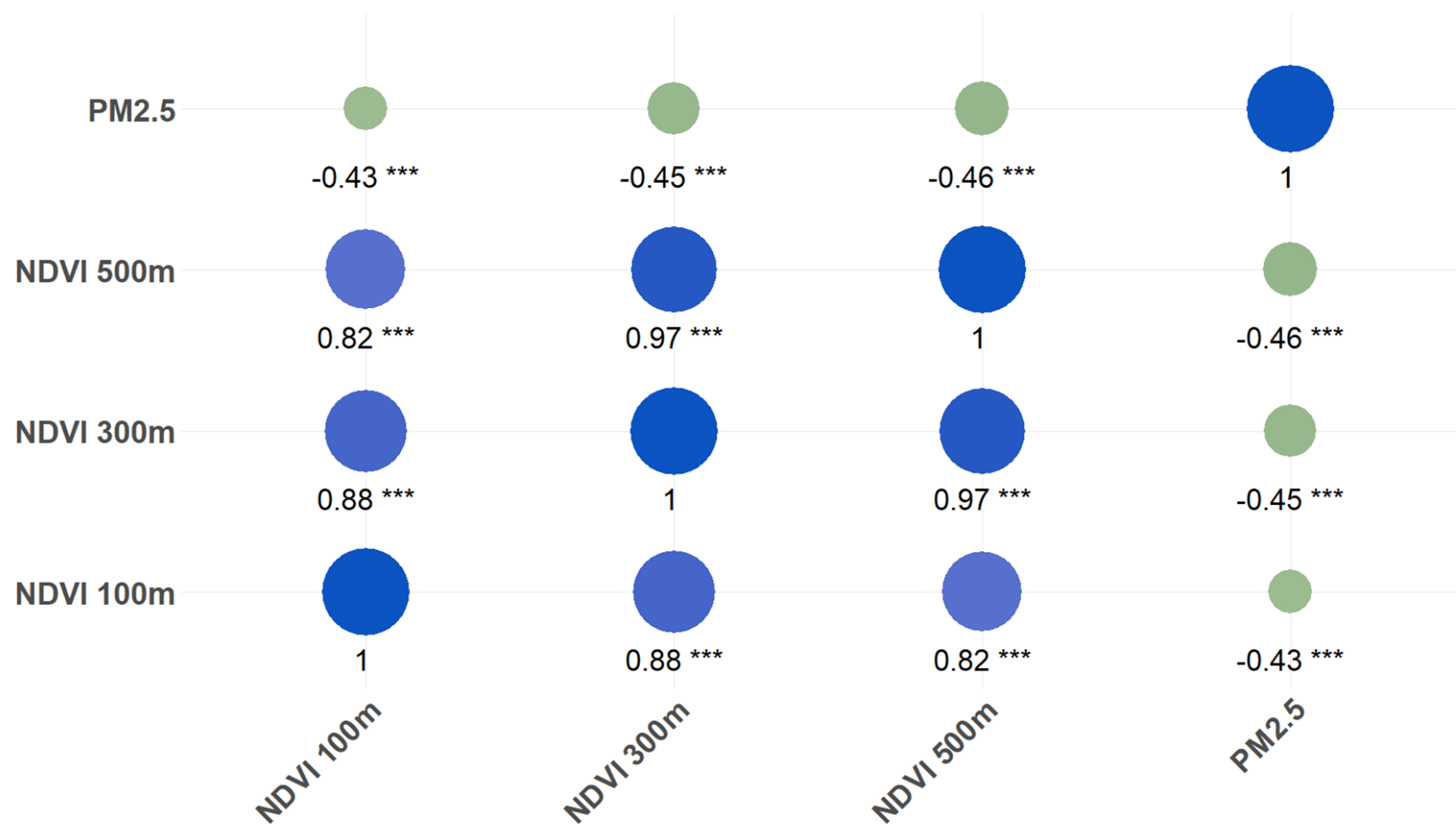
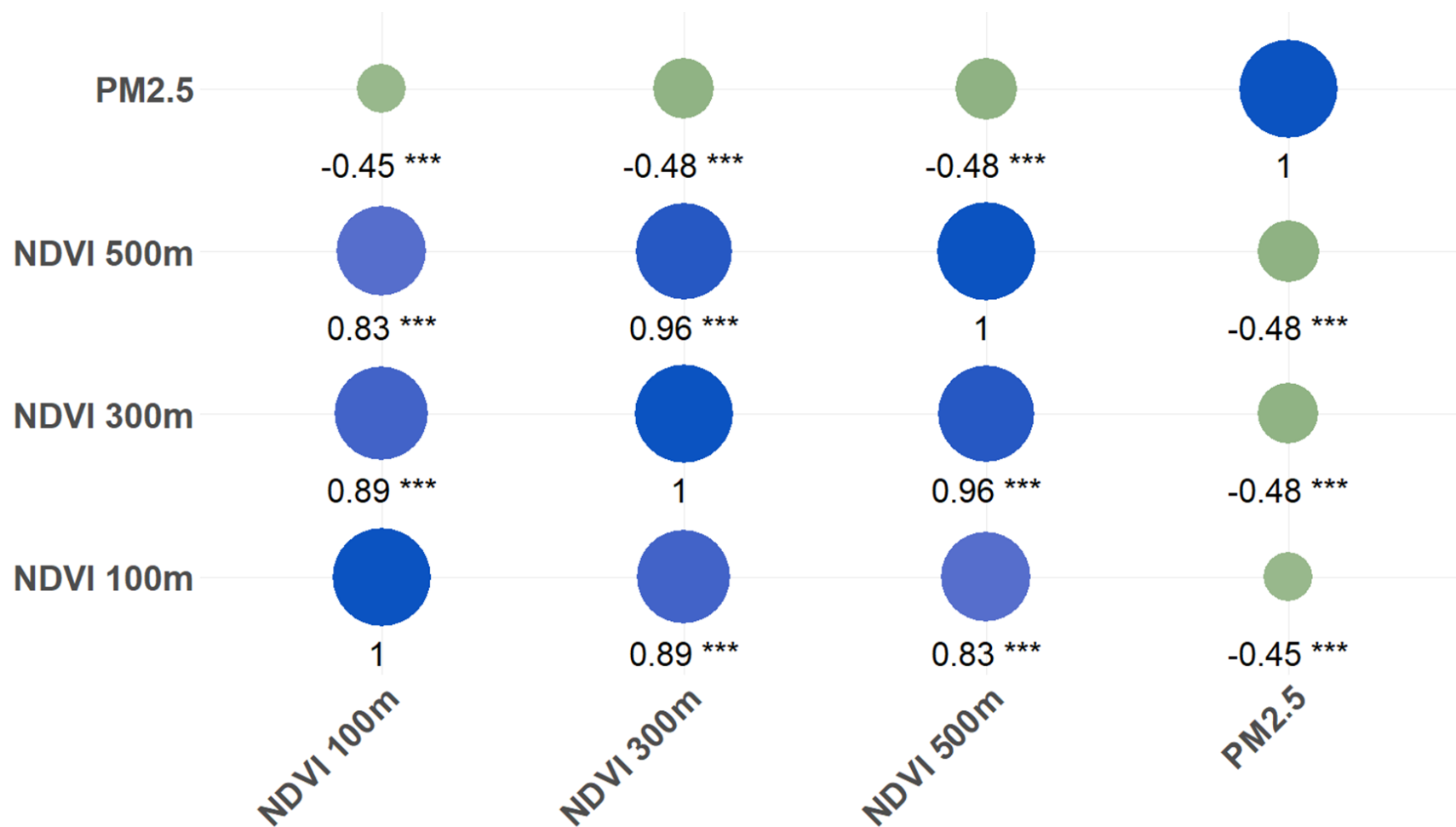


Figure S2. Correlation coefficients between the Normalized Difference Vegetation Index (NDVI) at 100-, 300-, and 500-meters, and outdoor PM_{2.5} during pregnancy for participants at the 6-year follow-up.



* p-value <0.05, ** p-value <0.001, *** p-value <0.0001. PM_{2.5} particulate matter with an aerodynamic diameter less than 2.5 μm.

Figure S3. Correlation coefficients between the Normalized Difference Vegetation Index (NDVI) at 100-, 300-, and 500-meters, and outdoor PM_{2.5} during pregnancy for participants at the 12-year follow-up.



* p-value <0.05, ** p-value <0.001, *** p-value <0.0001. PM_{2.5} particulate matter with an aerodynamic diameter less than 2.5 μm.

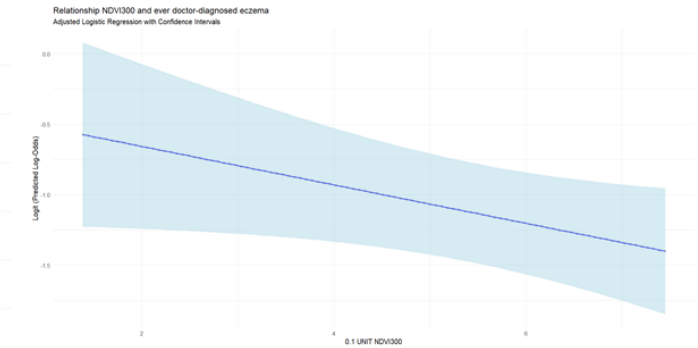
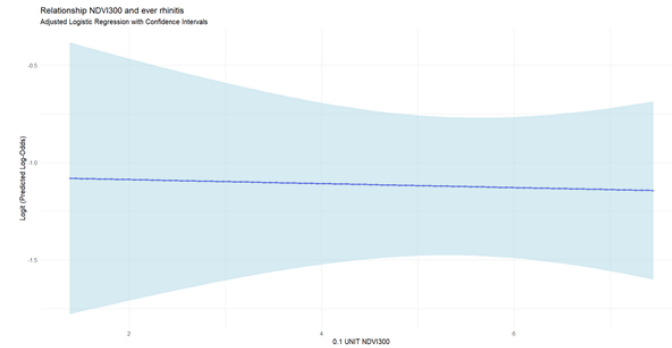
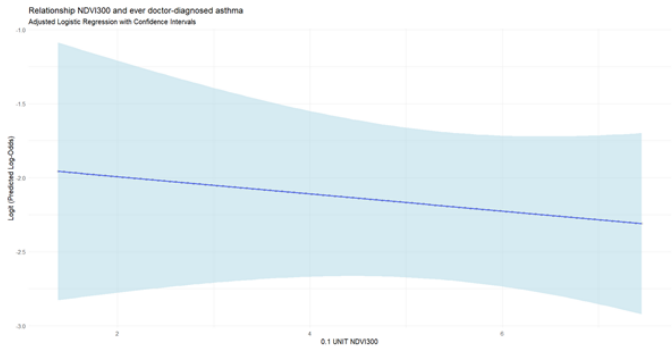
Figure S4. Relationship between NDVI 300m and ever doctor-diagnosed asthma, ever rhinitis, and ever doctor-diagnosed eczema at 6-year follow-up. Comparison of fully adjusted logistic regression models with and without restricted cubic splines.

Ever doctor-diagnosed asthma

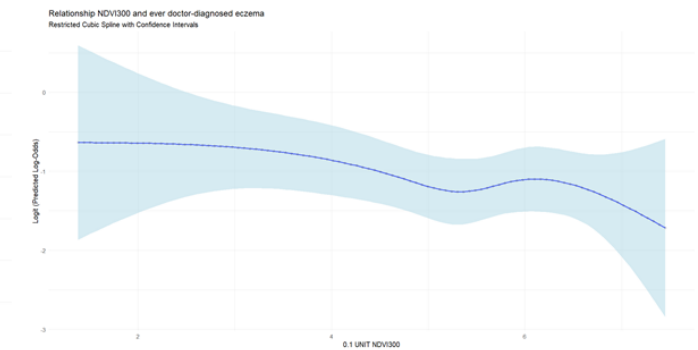
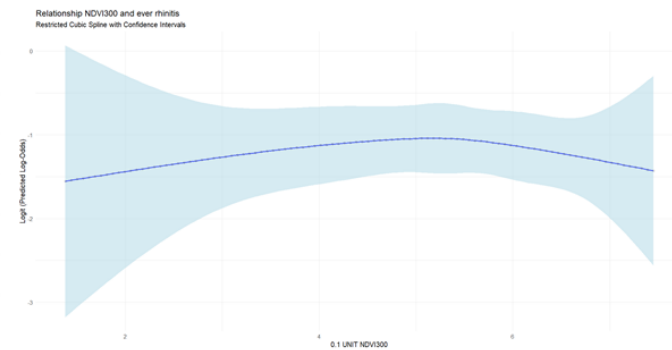
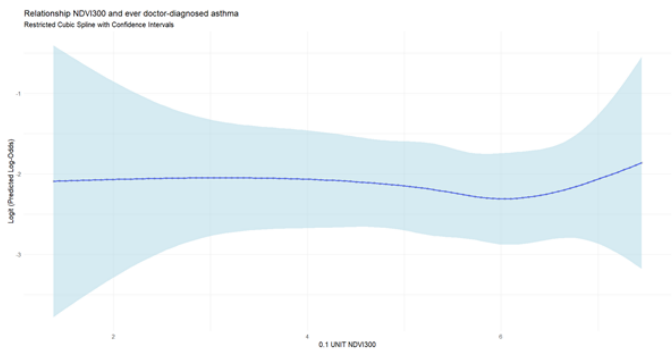
Ever rhinitis

Ever doctor-diagnosed eczema

Adjusted logistic regression



Restricted cubic splines



Likelihood ratio test of nested models
 $p = 0.88$

Likelihood ratio test of nested models
 $p = 0.71$

Likelihood ratio test of nested models
 $p = 0.55$

Figure S5. Relationship between NDVI 300m 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.

