

# Appendix - Urban environment and cognitive and motor function in children from four European birth cohorts

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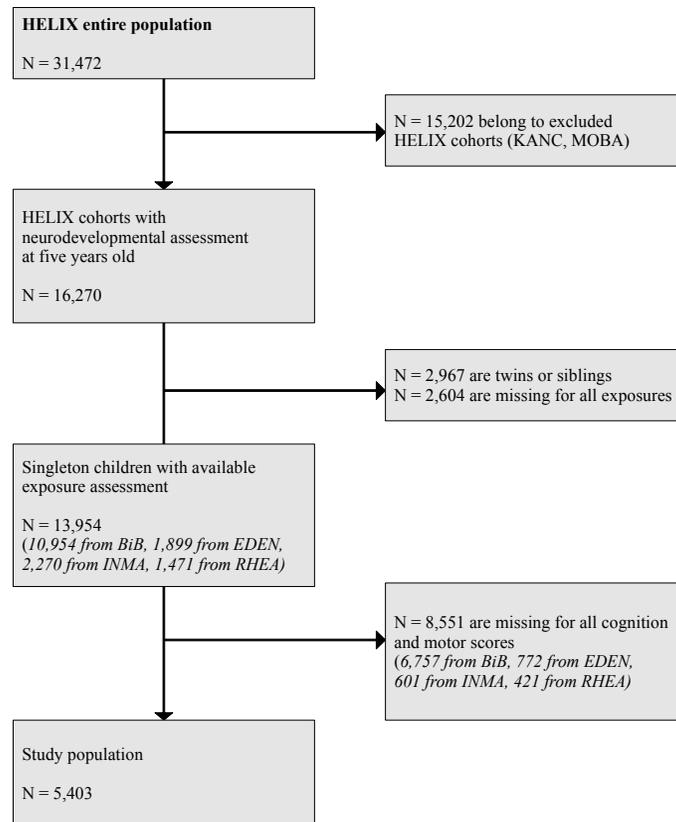
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# 1 Study population

## 1.1 Flowchart of inclusions

Figure S1: Flowchart of inclusions



KANC, Kaunas Cohort; MoBa, Norwegian Mother and Child Cohort Study.

## 2 Urban environment and socioeconomic characteristics

## 2.1 Data sources

**Table S1: Urban exposure data sources**

	<b>BiB (2007-2015)</b>	<b>EDEN (2003-2011)</b>	<b>INMA (2008-2013)</b>	<b>RHEA (2007-2013)</b>
Urban environment				
Building density	MasterMap (Ordinance Survey) (2013)	IGN (2014)	Geoskadi (2014) for Gipuzkoa ICC (2011) for Sabadell	Greek Statistical Authority (2001)
Street connectivity and Facilities	Navteq (2012)	Navteq (2012)	Generalitat Valenciana (Terrasit) (2007-2009) for Valencia	Navteq (2012)
Population density	EEA (2001)	EEA (2001)	Navteq (2012) Euskadi Government (2008) for Gipuzkoa	EEA (2001)
Public transport (bus stops)	Bradford Metropolitan District Council (2014, 2015)	Grand Nancy (2014) Grand Poitiers (2013)	INE (2011) for Sabadell and Valencia Disputation de Gipuzkoa (2011) Sabadell Municipality (2014) Open Street Maps (2015) for Valencia	Open Street Maps (2015)
Major green and blue spaces and land use	Urban Atlas (2006)	Urban Atlas (2006)	EUNIS and UDALPLAN (Departamento de Medio Ambiente y Política Territorial - Gobierno Vasco) (2009) for Gipuzkoa Urban Atlas (2006) for Sabadell and Valencia	Urban Atlas (2006)
NDVI			————— Landsat 4–5 TM, Landsat 7 ETM+, and Landsat 8 OLI/TIRS —————	
Air pollution				
NO <sub>2</sub>	ESCAPE local LUR	Local dispersion model	ESCAPE local LUR	ESCAPE local LUR
PM <sub>2.5</sub>	ESCAPE local LUR	ESCAPE European LUR	ESCAPE local LUR	ESCAPE local LUR

BiB, Born in Bradford; EDEN, Étude des Déterminants Pré et Postnataux du Développement et de la Santé de l'Enfant; EEA, European Environment Agency; ESCAPE, European Study of Cohorts for Air Pollution Effects; ETM+, Enhanced Thematic Mapper Plus; ICC, Institut Cartogràfic de Catalunya; IGN, Institut National de l'Information Géographique et Forestière (<http://professionnels.ign.fr>); INE, Instituto Nacional de Estadística; INMA, Infancia y Medio Ambiente; LUR, Land Use Regression; Navteq, ESRI Street Map for Mobile Navteq 2012; NDVI, Normalized Difference Vegetation Index; NO<sub>2</sub>, nitrogen dioxide; OLI, Operational Land Imager; PM<sub>2.5</sub>, particulate matter with an aerodynamic diameter of less than 2.5 µm; RHEA, Mother-Child Cohort in Crete; TIRS, Thermo Infrared Sensor; TM, Thematic Mapper.

**Table S2: Categories of facility density from Navteq<sup>1</sup>**

Categories	Sub-categories
Business	Business Facility, and Industrial zone
Community Services	City Hall, Civic/Community Center, County Council, Court House, Embassy, Government Office, Place of Worship, Police Station, and Post Office
Educational Institutions	Higher Education, Library, and School
Entertainment	Cinema, Nightlife, and Performing Arts
Financial Institutions	ATM, and Bank
Hospitals	Hospital, and Medical Service
Parks and Recreation	Amusement Park, Bowling Centre, Campground, Casino, Golf Course, Ice Skating Rink, Marina, Museum, Park/Recreation area, Public Sport Airport, Sports Centre, and Sports Complex
Restaurants	Coffee Shop, and Restaurant
Shopping	Bookstore, Clothing Store, Convenience Store, Customer Electronic Store, Department Store, Grocery Store, Hardware Store, Home Specialty Store, Office Supply, Pharmacy, Shopping, Speciality Store, and Sporting Goods
Transportation Hubs	Airport, Bus Station, Commuter Rail Station, Ferry Terminal, Train Station, Hotel, Other accommodation, Ski Lift, Winery

**Table S3: Categories of land use from Urban Atlas<sup>2</sup>**

Categories	Sub-classes	Definition
Artificial surfaces	Urban Fabric	Urban areas with dominant residential use or inner-city areas with central business district and residential use
	Industrial, commercial, public, military, private and transport units	Industrial, commercial, public, military and private units or transport units are predominant
	Mine, dump and construction sites	Strong human influence on soil surface, buildings not dominant
	Artificial non-agricultural vegetated areas	Leisure and recreation use dominates
Agricultural areas, semi-natural areas and wetlands		Little / no human influence, agriculture, forestry
Forests (natural and plantation)		Little / no human influence, agriculture, forestry
Water		

**Table S4: Socioeconomic data sources**

Cohort	Name	Source	Description	Year
BIB	Index of Multiple Deprivation (IMD)	Leeds City Council	Combines information from the seven domains to produce an overall relative measure of deprivation. The domains are combined using the following weights: income deprivation (22.5%), employment deprivation (22.5%), education, skills and training deprivation (13.5%), health deprivation and disability (13.5%), crime (9.3%), barriers to housing and services (9.3%), and living environment deprivation (9.3%)	2012
EDEN	French European deprivation index (EDI) score	Plate-forme méthodologique nationale pour l'étude et la réduction des inégalités sociales en cancérologie (ERISC)	Includes overcrowding, no access to a system of central or electric heating, non-owner, unemployment, foreign nationality, no access to a car, unskilled worker–farm worker, household with more than six, low level of education, and single-parent household.	2007
INMA	Urban vulnerability index	Spanish Statistical Office (INE)	Classification according to socioeconomic criteria, includes the whole of 5 socioeconomic indicators: percentage of unemployed population, percentage of unemployed youth population, percentage of employed persons eventual, percentage of unqualified employed persons, and percentage of population without studies	2001
RHEA	Deprivation index	ISGlobal based on data from Hellenic Statistical Authority	Calculated based on educational level	2001

BiB, Born in Bradford; EDEN, Étude des Déterminants Pré et Postnatals du Développement et de la Santé de l'Enfant; INMA, Infancia y Medio Ambiente; RHEA, Mother-Child Cohort in Crete.

## 2.2 Correlations between exposure indicators

Figure S2: Pairwise correlations between urban environment indicators during pregnancy

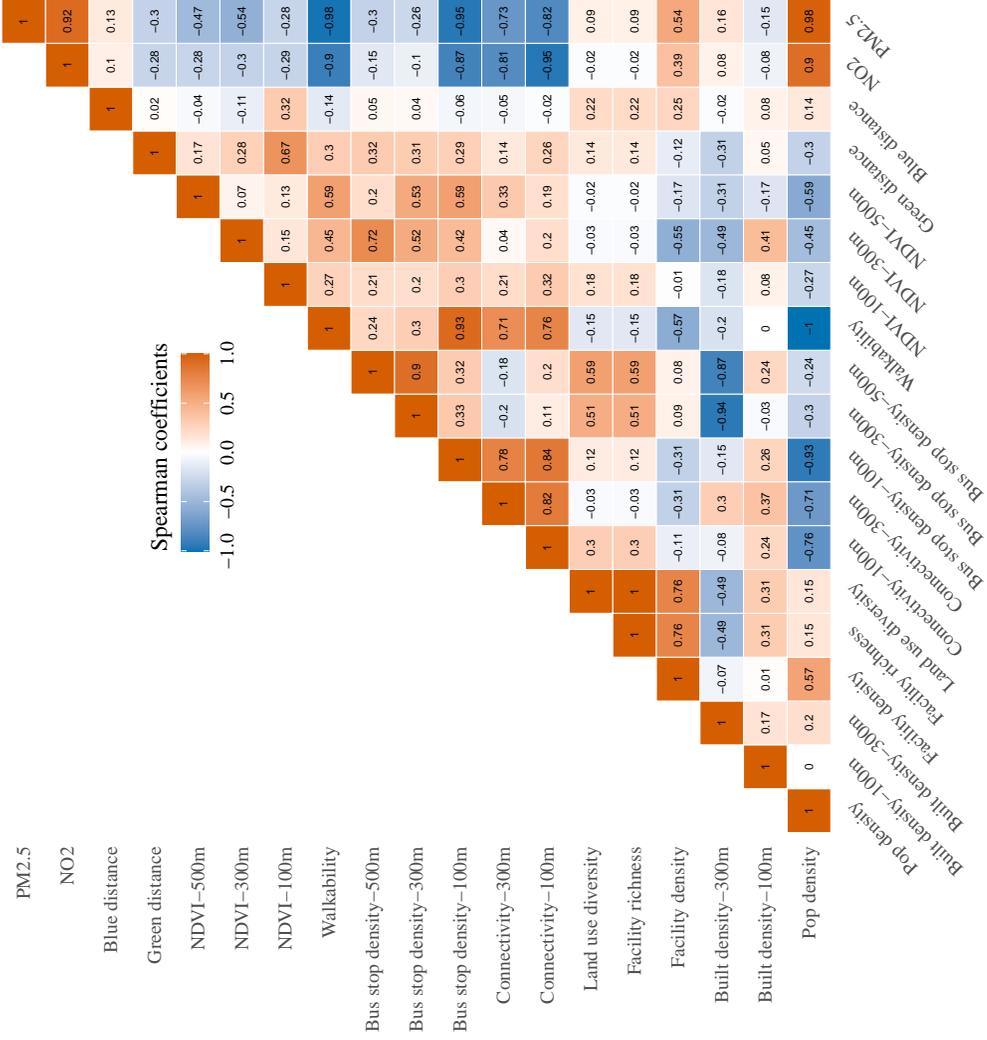
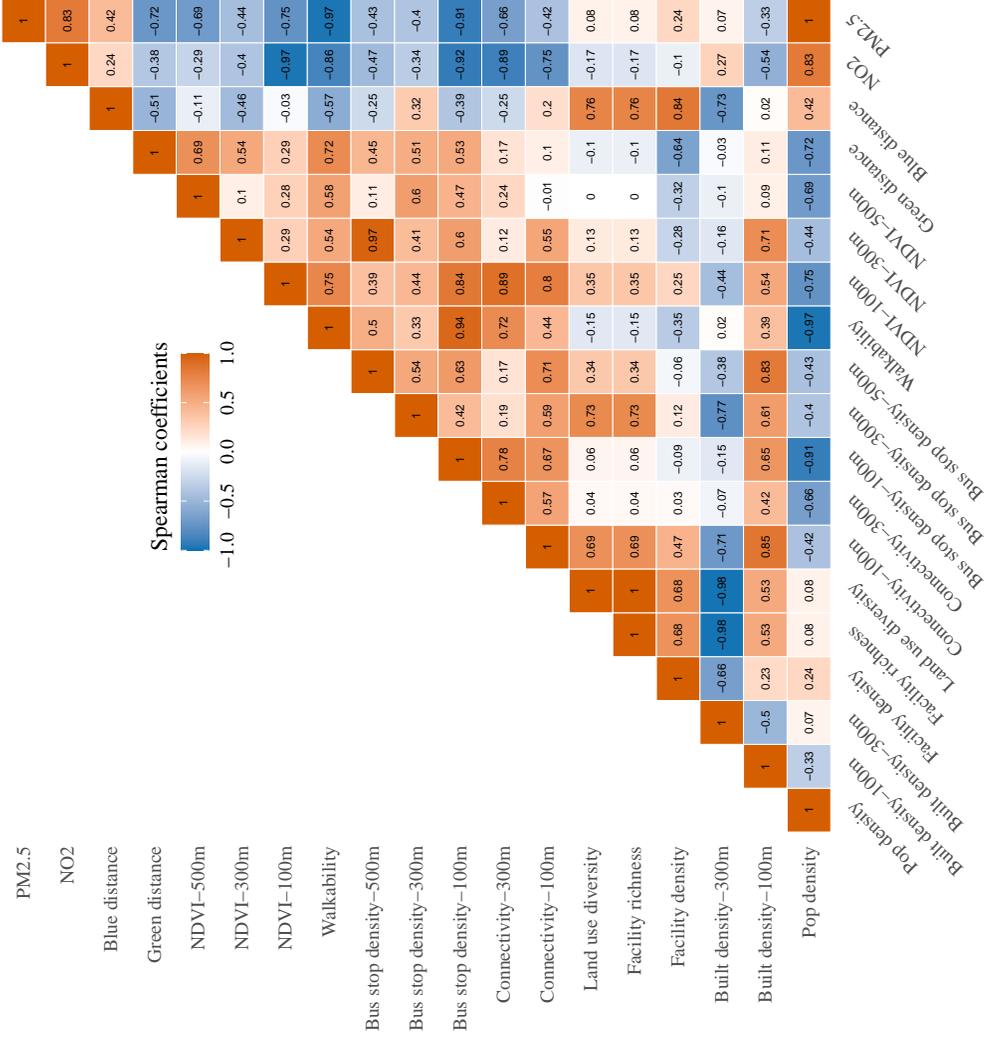
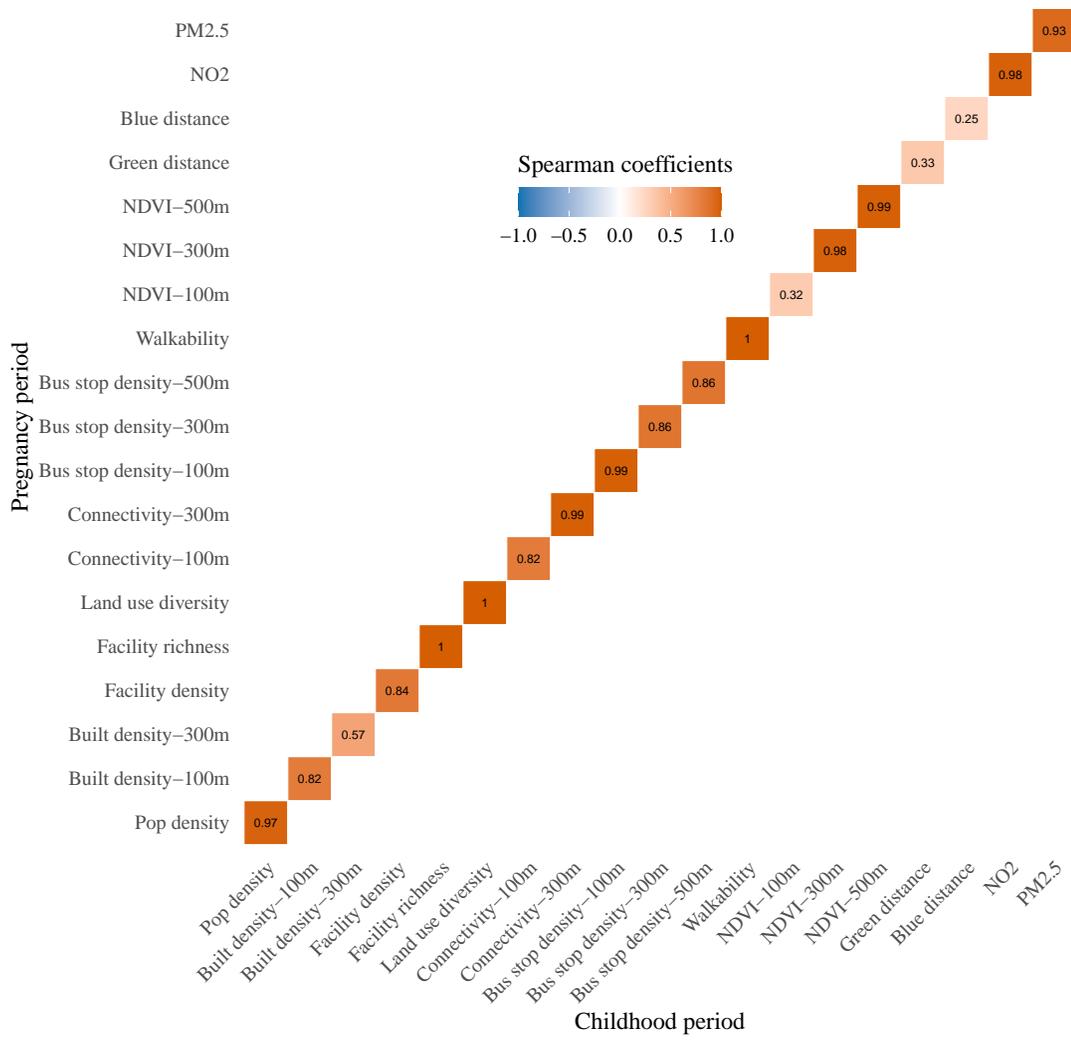


Figure S3: Pairwise correlations between urban environment indicators during childhood



NDVI, Normalized Difference Vegetation Index; NO2, nitrogen dioxide; PM2.5, particulate matter with an aerodynamic diameter of less than 2.5  $\mu\text{m}$ . Spearman coefficients are calculated over imputed- area-centered values.

**Figure S4: Correlations of urban environment indicators during pregnancy vs childhood**



NDVI, Normalized Difference Vegetation Index; NO2, nitrogen dioxide; PM2.5, particulate matter with an aerodynamic diameter of less than 2.5  $\mu\text{m}$ . Spearman coefficients are calculated over imputed- area-centered values.

**Table S5: Distribution of urban environment and socioeconomic variables in observed and imputed datasets**

	Observed dataset <sup>a</sup>	Imputed cognitive datasets (n = 5,364) <sup>a</sup>	Imputed motor datasets (n = 5,228) <sup>a</sup>	% data imputed
Built environment during pregnancy				
Population density (inhabitants/km <sup>2</sup> )	6857 ± 8044	6929 ± 8122	6945 ± 8214	1.2
Building density (m <sup>2</sup> /km <sup>2</sup> )				
100-m buffer	248184 ± 148598	246087 ± 146864	246746 ± 148206	8.7
300-m buffer	208783 ± 127204	206039 ± 125710	206299 ± 126948	7.8
Facility density (facilities/km <sup>2</sup> , 300-m buffer)	41.7 ± 60.5	41.7 ± 60.7	41.5 ± 61.1	1.1
Facility richness (facility types/km <sup>2</sup> , 300-m buffer)	0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.1	1.1
Land use diversity (300-m buffer)	0.5 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	9.9
Connectivity density (intersections/km <sup>2</sup> )				
100-m buffer	237.1 ± 147.3	232.7 ± 146.1	231.6 ± 145.6	9.8
300-m buffer	186.3 ± 95.3	181.4 ± 95.8	180.5 ± 95.8	7.4
Density of public bus stops (stops/km <sup>2</sup> )				
100-m buffer	28.6 ± 74.4	30.3 ± 82.0	30.8 ± 83.4	16.9
300-m buffer	25.8 ± 34.9	24.3 ± 33.5	24.2 ± 33.9	16.3
500-m buffer	22.4 ± 22.6	21.0 ± 21.9	20.9 ± 22.2	15.3
Walkability index (300-m buffer)	0.3 ± 0.1	0.3 ± 0.1	0.3 ± 0.1	13.1
Natural spaces during pregnancy				
NDVI				
100-m buffer	0.4 ± 0.1	0.3 ± 0.1	0.3 ± 0.1	1.2
300-m buffer	0.4 ± 0.1	0.4 ± 0.1	0.4 ± 0.1	1.2
500-m buffer	0.4 ± 0.1	0.4 ± 0.1	0.4 ± 0.1	1.2
Distance to nearest major green space (m)	185 ± 160	177 ± 158	176 ± 158	10.1
Distance to nearest major blue space (m)	1761 ± 1635	1748 ± 1617	1760 ± 1633	10.1
Air pollution during pregnancy				
NO <sub>2</sub> (µg/m <sup>3</sup> )	21.7 ± 10.3	21.6 ± 10.4	21.6 ± 10.5	9.2
PM <sub>2.5</sub> (µg/m <sup>3</sup> )	15.3 ± 3.3	15.3 ± 3.3	15.4 ± 3.3	1.2
Built environment during childhood				
Population density (inhabitants/km <sup>2</sup> )				
100-m buffer	6337 ± 7721	6392 ± 7782	6390 ± 7864	0.9
300-m buffer	236218 ± 147718	235267 ± 145814	236141 ± 147454	10.7
Facility density (facilities/km <sup>2</sup> , 300-m buffer)	196929 ± 126199	195961 ± 124787	196344 ± 125886	9.6
Facility richness (facility types/km <sup>2</sup> , 300-m buffer)	35.7 ± 49.6	35.9 ± 49.7	35.6 ± 50.1	0.4
Land use diversity (300-m buffer)	0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.1	0.4
Connectivity density (intersections/km <sup>2</sup> )	0.5 ± 0.1	0.5 ± 0.1	0.3 ± 0.1	31.2
100-m buffer	224.3 ± 145.5	218.6 ± 144.2	217.5 ± 144.1	12.3

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	Observed dataset <sup>a</sup>	Imputed cognitive datasets (n = 5,364) <sup>a</sup>	Imputed motor datasets (n = 5,228) <sup>a</sup>	% data imputed
300-m buffer	174.0 ± 93.1	171.7 ± 93.1	170.5 ± 92.8	9.4
Density of public bus stops (stops/km <sup>2</sup> )				
100-m buffer	27.6 ± 80.0	27.7 ± 82.6	27.8 ± 92.8	19.3
300-m buffer	24.9 ± 35.1	22.8 ± 33.1	22.6 ± 33.6	18.5
500-m buffer	21.8 ± 22.9	20.0 ± 22.0	19.8 ± 22.1	17.7
Walkability index (300-m buffer)	0.3 ± 0.1	0.3 ± 0.1	0.3 ± 0.1	35.8
Natural spaces during childhood				
NDVI 100-m buffer	0.4 ± 0.1	0.4 ± 0.1	0.4 ± 0.1	1.3
300-m buffer	0.4 ± 0.1	0.4 ± 0.1	0.4 ± 0.1	1.3
500-m buffer	0.4 ± 0.1	0.4 ± 0.1	0.4 ± 0.1	1.3
Distance to nearest major green space (m)	170 ± 156	162 ± 153	161 ± 153	11.3
Distance to nearest major blue space (m)	1772 ± 1634	1794 ± 1688	1794 ± 1681	11.3
Air pollution during childhood				
NO <sub>2</sub> (µg/m <sup>3</sup> )	25.1 ± 11.6	25.1 ± 11.7	25.0 ± 11.7	0.7
PM <sub>2.5</sub> (µg/m <sup>3</sup> )	15.1 ± 2.7	15.2 ± 2.7	15.2 ± 2.7	0.7
Parental characteristics				
Parents country of birth				0.8
none or one in the country of inclusion	1707 (31.8%)	1711 (31.2%)	1592 (31.2%)	
both	3654 (68.2%)	3653 (68.8%)	3636 (68.8%)	
Deprivation index at area-level during pregnancy				11.3
less deprived	1397 (29.1%)	1611 (30.4%)	1611 (30.4%)	
middle deprived	1734 (36.2%)	1932 (35.9%)	1874 (35.9%)	
most deprived	1662 (35.7%)	1821 (33.7%)	1743 (33.7%)	
Deprivation index at area-level at four- to five-years old				11.5
less deprived	1521 (31.8%)	1723 (32.5%)	1720 (32.5%)	
middle deprived	1786 (37.3%)	1994 (37.1%)	1931 (37.1%)	
most deprived	1477 (30.9%)	1647 (30.4%)	1577 (30.4%)	
Maternal age (years)	29.8 ± 5.2	29.8 ± 5.2	29.8 ± 5.2	0.6
Maternal educational level				4.0
less than primary, primary, and lower secondary	1610 (31.0%)	1708 (31.3%)	1607 (31.3%)	
upper secondary, and post-secondary non-tertiary	1695 (32.7%)	1734 (32.6%)	1717 (32.6%)	
tertiary	1884 (36.3%)	1922 (36.1%)	1904 (36.1%)	
Maternal pre-pregnancy body mass index (kg/m <sup>2</sup> )	25.4 ± 5.4	25.4 ± 5.4	25.4 ± 5.4	2.1
Parity				2.5
no child	2328 (44.2%)	2363 (44.3%)	2327 (44.3%)	
1 child	1802 (34.2%)	1835 (34.3%)	1799 (34.3%)	
≥ 2 children	1140 (21.6%)	1166 (21.4%)	1102 (21.4%)	
Maternal smoking during pregnancy				3.3
no	4094 (78.3%)	4209 (78.3%)	4086 (78.3%)	

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	Observed dataset <sup>a</sup>	Imputed cognitive datasets (n = 5,364) <sup>a</sup>	Imputed motor datasets (n = 5,228) <sup>a</sup>	% data imputed
yes	1133 (21.7%)	1155 (21.7%)	1142 (21.7%)	
Paternal age (years)	33.5 ± 5.3	33.5 ± 5.7	33.4 ± 5.7	40.6
Paternal educational level				12.1
less than primary, primary, and lower secondary	1568 (33.0%)	1914 (35.4%)	1832 (35.4%)	
upper secondary, and post-secondary non-tertiary	1702 (35.9%)	1821 (34.3%)	1812 (34.3%)	
tertiary	1477 (31.1%)	1629 (30.3%)	1584 (30.3%)	
Paternal body mass index				43.6
<25 kg/m <sup>2</sup>	1280 (42.0%)	1865 (34.9%)	1830 (34.9%)	
25-29 kg/m <sup>2</sup>	1354 (44.4%)	2273 (42.5%)	2227 (42.5%)	
≥ 30 kg/m <sup>2</sup>	413 (13.6%)	1226 (22.6%)	1171 (22.6%)	
Child characteristics				
Season of birth				0.4
winter	1316 (24.5%)	1315 (24.5%)	1281 (24.5%)	
spring	1369 (25.5%)	1362 (25.4%)	1325 (25.4%)	
summer	1320 (24.5%)	1316 (24.4%)	1266 (24.4%)	
autumn	1374 (25.5%)	1371 (25.7%)	1356 (25.7%)	
Child sex				0.0
female	2615 (48.4%)	2595 (48.5%)	2543 (48.5%)	
male	2786 (51.6%)	2762 (51.5%)	2685 (51.5%)	
Child age at cognitive assessment (days)	1830 ± 218	1830 ± 217	—	0.4
Child age at motor assessment (days)	1831 ± 218	—	1831 ± 219	1.0

NDVI, Normalized Difference Vegetation Index; NO<sub>2</sub>, nitrogen dioxide; PM<sub>2.5</sub>, particulate matter with an aerodynamic diameter of less than 2.5 μm.

<sup>a</sup> mean ± sd or N (%). Statistics for imputed datasets are aggregated using Rubin's rules.

### 2.3 Description of urban environment and socioeconomic variables

Table S6: Description of the urban environment, socioeconomic and family variables in each HELIX cohort.

	Mean ± sd or N (%) <sup>a</sup>							
	All (N=5,403)	BIB - UK (N=2,078)	EDEN, Nancy - France (N=487)	EDEN, Poitiers - France (N=639)	INMA, Gipuzkoa - Spain (N=391)	INMA, Sabadell - Spain (N = 500)	INMA, Valencia - Spain (N=529)	RHEA - Greece (N=779)
Built environment during pregnancy								
Population density (inhabitants/km <sup>2</sup> ) <sup>b</sup>	6857 ± 8044	5489 ± 1937	3537 ± 3617	1479 ± 2053	8350 ± 8325	18618 ± 13771	12716 ± 13187	5608 ± 4764
Building density (m <sup>2</sup> /km <sup>2</sup> ) <sup>b</sup>								
100-m buffer	248184 ± 148598	197384 ± 66093	213300 ± 115031	144000 ± 94528	213077 ± 96919	405072 ± 166438	443137 ± 188710	306846 ± 141765
300-m buffer	208783 ± 127204	176319 ± 55823	162707 ± 99235	103927 ± 77846	162986 ± 71931	361474 ± 142041	362934 ± 157853	257226 ± 122661
Facility density (facilities/km <sup>2</sup> , 300-m buffer) <sup>c</sup>	41.7 ± 60.5	42.7 ± 36.7	30.6 ± 83.5	17.7 ± 70.6	37.0 ± 57.4	53.9 ± 57.8	44.4 ± 59.4	59.0 ± 79.0
Facility richness (facility types/km <sup>2</sup> , 300-m buffer)	0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.1
Land use diversity (300-m buffer)	0.5 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	0.4 ± 0.1	0.5 ± 0.1	0.4 ± 0.1
Connectivity density (intersections/km <sup>2</sup> ) <sup>b</sup>								
100-m buffer	237.1 ± 147.3	251.6 ± 150.4	194.4 ± 136.5	208.5 ± 148.0	225.2 ± 136.9	222.6 ± 112.0	249.9 ± 140.0	267.1 ± 173.5
300-m buffer	186.3 ± 95.3	200.7 ± 88.3	146.3 ± 80.0	148.5 ± 104.1	169.3 ± 69.9	199.9 ± 57.3	192.6 ± 84.4	208.4 ± 145.2
Density of public bus stops (stops/km <sup>2</sup> ) <sup>c</sup>								
100-m buffer	28.6 ± 74.4	28.1 ± 34.6	18.2 ± 29.4	27.9 ± 37.9	89.9 ± 203.7	26.6 ± 30.2	33.3 ± 97.0	1.9 ± 8.4
300-m buffer	25.8 ± 34.9	26.2 ± 11.8	16.2 ± 12.6	21.3 ± 16.1	73.3 ± 77.0	23.9 ± 9.7	36.1 ± 61.1	1.5 ± 3.2
500-m buffer	22.4 ± 22.6	24.6 ± 8.3	14.6 ± 9.9	19.3 ± 11.2	52.1 ± 42.9	21.2 ± 5.5	29.7 ± 40.2	1.4 ± 2.2
Walkability index (300-m buffer)	0.3 ± 0.1	0.3 ± 0.1	0.3 ± 0.1	0.2 ± 0.1	0.3 ± 0.1	0.3 ± 0.1	0.3 ± 0.1	0.3 ± 0.1
Natural spaces during pregnancy								
NDVI								
100-m buffer	0.4 ± 0.1	0.4 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	0.4 ± 0.1	0.2 ± 0.1	0.2 ± 0.1	0.2 ± 0.1
300-m buffer	0.4 ± 0.1	0.4 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	0.2 ± 0.1	0.2 ± 0.1	0.2 ± 0.1
500-m buffer	0.4 ± 0.1	0.4 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	0.3 ± 0.1	0.3 ± 0.1	0.3 ± 0.1
Distance to nearest major green space (m) <sup>c</sup>	185 ± 160	215 ± 158	146 ± 140	116 ± 135	96 ± 76	243 ± 215	138 ± 108	218 ± 172.5
Distance to nearest major blue space (m) <sup>c</sup>	1761 ± 1635	1843 ± 1083	1410 ± 1587	1357 ± 1035	266 ± 399	1107 ± 623	3191 ± 1869	2299 ± 2848
Air pollution during pregnancy								
NO <sub>2</sub> (µg/m <sup>3</sup> ) <sup>c</sup>	21.7 ± 10.3	20.4 ± 3.2	30.1 ± 10.5	15.4 ± 5.2	19.0 ± 4.5	43.1 ± 11.0	24.2 ± 10.4	12.5 ± 4.9
PM <sub>2.5</sub> (µg/m <sup>3</sup> )	15.3 ± 3.3	13.5 ± 1.8	23.6 ± 1.7	17.5 ± 1.8	14.3 ± 0.7	15.1 ± 1.8	14.5 ± 1.5	14.5 ± 1.3
Built environment during childhood								
Population density (inhabitants/km <sup>2</sup> ) <sup>b</sup>	6337 ± 7721	5289 ± 1966	2664 ± 3070	1129 ± 1514	8090 ± 8275	15848 ± 13238	11672 ± 13013	5236 ± 4752
Building density (m <sup>2</sup> /km <sup>2</sup> ) <sup>b</sup>								
100-m buffer	236218 ± 147718	187455 ± 64525	191016 ± 100032	125717 ± 83243	210565 ± 97564	388193 ± 174284	425366 ± 193867	295069 ± 138894
300-m buffer	196929 ± 126199	168027 ± 56280	135481 ± 81180	85839 ± 65519	162143 ± 73591	345984 ± 149812	343822 ± 160367	245892 ± 119948

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	Mean ± sd or N (%) <sup>a</sup>									
All (N=5,403)	BIB - UK (N=2,078)	EDEN, Nancy - France (N=487)	EDEN, Poitiers - France (N=639)	INMA, Gipuzkoa - Spain (N=391)	INMA, Sabadell - Spain (N=500)	INMA, Valencia - Spain (N=529)	RHEA - Greece (N=779)			
Facility density (facilities/km <sup>2</sup> , 300-m buffer) <sup>c</sup>	38.0 ± 34.9	17.8 ± 50.3	9.6 ± 38.9	37.1 ± 57.9	48.1 ± 55.6	41.2 ± 56.9	50.4 ± 63.8			
Facility richness (facility types/km <sup>2</sup> , 300-m buffer)	0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.1			
Land use diversity (300-m buffer)	0.5 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	0.4 ± 0.1	0.5 ± 0.1	0.4 ± 0.1			
Connectivity density (intersections/km <sup>2</sup> ) <sup>b</sup>										
100-m buffer	237.5 ± 149.7	184.0 ± 128.9	176.7 ± 135.7	221.1 ± 134.9	219.3 ± 117.4	243.8 ± 142.2	256.4 ± 170.7			
300-m buffer	189.9 ± 86.3	128.1 ± 75.4	122.5 ± 90.9	166.3 ± 70.5	193.8 ± 63.7	183.5 ± 86.9	196.5 ± 138.7			
Density of public bus stops (stops/km <sup>2</sup> ) <sup>c</sup>										
100-m buffer	25.0 ± 33.1	15.2 ± 29.0	19.7 ± 32.4	93.0 ± 209.1	26.2 ± 29.8	39.8 ± 129.1	1.7 ± 8.1			
300-m buffer	25.3 ± 12.1	13.2 ± 12.0	17.2 ± 15.4	71.8 ± 78.4	23.1 ± 10.1	35.2 ± 58.3	1.3 ± 3.0			
500-m buffer	23.9 ± 8.5	11.9 ± 9.7	16.3 ± 10.8	51.8 ± 43.2	20.3 ± 6.2	29.9 ± 40.2	1.2 ± 2.0			
Walkability index (300-m buffer)	0.3 ± 0.1	0.3 ± 0.1	0.3 ± 0.1	0.3 ± 0.1	0.4 ± 0.1	0.4 ± 0.1	0.4 ± 0.1			
Natural spaces during childhood										
NDVI 100-m buffer	0.4 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	0.4 ± 0.1	0.2 ± 0.1	0.2 ± 0.1	0.2 ± 0.1			
300-m buffer	0.4 ± 0.1	0.6 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	0.3 ± 0.1	0.2 ± 0.1	0.2 ± 0.1			
500-m buffer	0.4 ± 0.1	0.6 ± 0.1	0.6 ± 0.1	0.5 ± 0.1	0.3 ± 0.1	0.3 ± 0.1	0.3 ± 0.1			
Distance to nearest major green space (m) <sup>c</sup>	196 ± 153	127 ± 129	84 ± 115	95 ± 78	229 ± 205	129 ± 103.8	206 ± 177			
Distance to nearest major blue space (m) <sup>c</sup>	1793 ± 1062	1476 ± 1573	1458 ± 1000	270 ± 408	1178 ± 681	3156 ± 1897	2430 ± 2884			
Air pollution during childhood										
NO <sub>2</sub> (µg/m <sup>3</sup> ) <sup>c</sup>	30.3 ± 4.5	24.2 ± 7.5	12.9 ± 3.1	14.2 ± 2.6	37.9 ± 13.0	32.8 ± 16.0	13.9 ± 5.3			
PM <sub>2.5</sub> (µg/m <sup>3</sup> )	13.7 ± 1.5	21.2 ± 0.9	16.4 ± 0.8	12.3 ± 0.8	15.1 ± 2.0	13.7 ± 1.2	16.7 ± 1.9			
Parental characteristics										
Parents country of birth										
none or one in the country of inclusion	1383 (67.0%)	46 (9.5%)	60 (9.6%)	11 (2.8%)	75 (15.3%)	76 (14.4%)	56 (7.2%)			
both	682 (33.0%)	436 (90.5%)	568 (90.4%)	380 (97.2%)	416 (84.7%)	453 (85.6%)	719 (92.8%)			
Deprivation index at area-level during pregnancy <sup>d</sup>										
less deprived	176 (8.9%)	169 (34.9%)	301 (48.3%)	323 (82.8%)	164 (37.1%)	123 (23.3%)	141 (41.7%)			
middle deprived	753 (37.9%)	116 (23.9%)	164 (26.3%)	67 (17.2%)	197 (44.6%)	327 (61.8)	110 (32.5%)			
most deprived	1057 (53.2%)	200 (41.2%)	158 (25.4%)	0	81 (18.3%)	79 (14.9%)	87 (25.7%)			
Deprivation index at area-level at four- to five- years old <sup>d</sup>										
less deprived	187 (9.6%)	186 (38.8%)	321 (53.8%)	326 (83.4%)	228 (46.9%)	131 (24.8%)	142 (40.2%)			
middle deprived	819 (42.0%)	122 (35.8%)	157 (26.3%)	65 (16.6%)	184 (37.9%)	316 (59.8%)	123 (34.8%)			
most deprived	943 (48.4%)	172 (35.8%)	119 (19.9%)	0	74 (15.2%)	81 (15.3%)	88 (24.9%)			
Maternal age (years)	28.1 ± 5.7	30.0 ± 4.6	29.8 ± 4.8	32.8 ± 3.8	31.8 ± 4.2	31.8 ± 4.2	30.3 ± 4.9			
Maternal educational level <sup>e</sup>										
less than primary, primary, and lower secondary	1214 (85.5%)	13 (2.7%)	36 (5.7%)	46 (11.8%)	115 (24.3%)	147 (27.8%)	39 (5.0%)			
upper secondary, and post-secondary non-tertiary	1695 (32.7%)	144 (29.8%)	273 (43.5%)	142 (36.4%)	203 (42.8%)	232 (43.9%)	435 (56.1%)			

Continued on next page

	Mean ± sd or N (%) <sup>a</sup>									
	All (N=5,403)	BIB - UK (N=2,078)	EDEN, Nancy - France (N=487)	EDEN, Poitiers - France (N=639)	INMA, Spain (N=391)	Gipuzkoa - INMA, Sabadell - Spain (N = 500)	INMA, Valencia - Spain (N=529)	RHEA - Greece (N=779)		
<i>tertiary</i>	1884 (36.3%)	430 (22.5%)	327 (67.6%)	318 (50.7%)	202 (51.8%)	156 (32.9%)	150 (29.4%)	301 (38.8%)		
Maternal pre-pregnancy body mass index (kg/m <sup>2</sup> )	25.4 ± 5.4	28.2 ± 5.5	23.4 ± 4.8	23.4 ± 4.6	22.8 ± 3.5	23.8 ± 4.6	23.8 ± 4.4	24.5 ± 4.8		
Parity										
<i>no child</i>	2328 (44.2%)	696 (34.9%)	211 (43.3%)	305 (47.9%)	220 (56.3%)	280 (58.9%)	289 (54.6%)	327 (43.3%)		
<i>1 child</i>	1802 (34.2%)	594 (29.8%)	183 (37.6%)	219 (34.4%)	149 (38.1%)	167 (35.2%)	202 (38.2%)	288 (38.1%)		
≥ 2 children	1140 (21.6%)	705 (35.3%)	93 (19.1%)	113 (17.7%)	22 (5.6%)	28 (5.9%)	38 (7.2%)	141 (18.7%)		
Maternal smoking during pregnancy										
<i>no</i>	4094 (78.3%)	1647 (84.5%)	401 (82.5%)	471 (74.2%)	294 (77.4%)	342 (72.6%)	327 (61.8%)	612 (78.7%)		
<i>yes</i>	1133 (21.7%)	301 (15.5%)	85 (17.5%)	164 (25.8%)	86 (22.6%)	129 (27.4%)	202 (38.2%)	166 (21.3%)		
Paternal age (years)	33.5 ± 5.3	NA	32.4 ± 5.4	32 ± 5.7	35.1 ± 4.3	33.6 ± 4.7	33.4 ± 4.8	34.4 ± 5.6		
Paternal educational level <sup>e</sup>										
<i>less than primary, primary, and lower secondary</i>	1568 (33.0%)	896 (57.8%)	30 (6.8%)	58 (9.6%)	85 (22.0%)	160 (33.8%)	234 (44.4%)	105 (13.7%)		
<i>upper secondary, and post-secondary non-tertiary</i>	1702 (35.9%)	196 (12.7%)	169 (38.6%)	296 (49.0%)	193 (49.9%)	203 (42.9%)	204 (38.7%)	441 (57.3%)		
<i>tertiary</i>	1477 (31.1%)	457 (29.5%)	239 (54.6%)	250 (41.4%)	109 (28.3%)	110 (23.6%)	89 (16.9%)	223 (29.0%)		
Paternal body mass index										
<25 kg/m <sup>2</sup>	1280 (42.0%)	NA	228 (54.3%)	215 (45.1%)	184 (48.3%)	219 (46.6%)	227 (42.9%)	207 (26.9%)		
25-29 kg/m <sup>2</sup>	1354 (44.4%)	NA	162 (38.6%)	204 (42.8%)	168 (44.1%)	190 (40.4%)	240 (45.4%)	390 (50.6%)		
≥ 30 kg/m <sup>2</sup>	413 (13.6%)	NA	30 (7.1%)	58 (12.2%)	29 (7.6%)	61 (13.0%)	62 (11.7%)	173 (22.5%)		
Child characteristics										
Season of birth										
<i>winter</i>	1316 (24.5%)	488 (23.5%)	101 (20.7%)	126 (19.7%)	99 (25.3%)	124 (26.0%)	148 (28.0%)	230 (29.6%)		
<i>spring</i>	1369 (25.5%)	546 (26.2%)	192 (39.4%)	131 (20.5%)	112 (28.6%)	121 (25.4%)	96 (18.1%)	171 (22.0%)		
<i>summer</i>	1320 (24.5%)	544 (26.2%)	116 (23.8%)	187 (29.3%)	108 (27.6%)	115 (24.1%)	108 (20.4%)	142 (18.3%)		
<i>autumn</i>	1374 (25.5%)	500 (24.1%)	78 (16.0%)	195 (30.5%)	72 (18.4%)	117 (24.5%)	177 (33.5%)	235 (30.2%)		
Child sex										
<i>female</i>	2615 (48.4%)	1028 (49.5%)	246 (50.5%)	280 (43.8%)	197 (50.6%)	243 (48.6%)	256 (48.4%)	365 (46.9%)		
<i>male</i>	2786 (51.6%)	1050 (50.5%)	241 (49.5%)	359 (56.2%)	192 (49.4%)	257 (51.4%)	273 (51.6%)	414 (53.1%)		

BiB, Born in Bradford; EDEN, Étude des Déterminants Pré et Postnataux du Développement et de la Santé de l'Enfant; INMA, Infancia y Medio Ambiente; NA, non available; NDVI, Normalized Difference Vegetation Index; NO<sub>2</sub>, nitrogen dioxide; PM<sub>2.5</sub>, particulate matter with an aerodynamic diameter of less than 2.5 μm; RHEA, Mother-Child Cohort in Crete.

<sup>a</sup> Distribution is displayed over non-imputed, non-transformed values.

<sup>b</sup> Square-root transformed.

<sup>c</sup> Ln-transformed.

<sup>d</sup> Socioeconomic level was described using deprivation indexes from each country and categorized into tertiles. More details are provided in Table S2.

<sup>e</sup> Education was defined using the International Standard Classification of Education (ISCED).

## 2.4 Description of urban environment and socioeconomic variables between participants and non-participants

**Table S7: Description of the urban environment, socioeconomic and family variables in each HELIX cohort.**

	Mean ± sd or N (%) <sup>a</sup>		P.value
	Participants (N=5403)	Non-Participants (N=8551)	
<b>Built environment during pregnancy</b>			
Population density (inhabitants/km <sup>2</sup> )	6857.7 ± 8044	5598.1 ± 4668.5	<0.001
missing	65 (1.2 %)	26 (0.3 %)	
Building density (m <sup>2</sup> /km <sup>2</sup> )			
100-m buffer	248183.8 ± 148598.4	210282.4 ± 104336.9	<0.001
missing	468 (8.7 %)	825 (9.6 %)	
300-m buffer	208783.4 ± 127204.1	181610.4 ± 88664.8	<0.001
missing	421 (7.8 %)	692 (8.1 %)	
Facility density (facilities/km <sup>2</sup> , 300-m buffer)	41.7 ± 60.5	41 ± 50.2	0.49
missing	62 (1.1 %)	25 (0.3 %)	
Facility richness (facility types/km <sup>2</sup> , 300-m buffer)	0.1 ± 0.1	0.1 ± 0.1	0.002
missing	62 (1.1 %)	25 (0.3 %)	
Land use diversity (300-m buffer)	0.5 ± 0.1	0.5 ± 0.1	0.255
missing	537 (9.9 %)	334 (3.9 %)	
Connectivity density (intersections/km <sup>2</sup> )			
100-m buffer	237.1 ± 147.3	241 ± 150.3	0.152
missing	532 (9.8 %)	375 (4.4 %)	
300-m buffer	186.3 ± 95.3	189.9 ± 90.8	0.034
missing	398 (7.4 %)	233 (2.7 %)	
Density of public bus stops (stops/km <sup>2</sup> )			
100-m buffer	28.6 ± 74.4	25.9 ± 48	0.025
missing	912 (16.9 %)	496 (5.8 %)	
300-m buffer	25.8 ± 34.9	24.8 ± 21.2	0.071
missing	879 (16.3 %)	477 (5.6 %)	
500-m buffer	22.4 ± 22.6	22.7 ± 14.1	0.341
missing	825 (15.3 %)	459 (5.4 %)	
Walkability index (300-m buffer)	0.3 ± 0.1	0.3 ± 0.1	<0.001
missing	709 (13.1 %)	424 (5 %)	
<b>Natural spaces during pregnancy</b>			
NDVI			
100-m buffer	0.4 ± 0.1	0.4 ± 0.1	<0.001
missing	67 (1.2 %)	31 (0.4 %)	
300-m buffer	0.4 ± 0.1	0.4 ± 0.1	<0.001
missing	67 (1.2 %)	31 (0.4 %)	
500-m buffer	0.4 ± 0.1	0.4 ± 0.1	<0.001
missing	67 (1.2 %)	31 (0.4 %)	
Distance to nearest major green space (m)	185.2 ± 160.3	190.1 ± 152.6	0.088
missing	547 (10.1 %)	334 (3.9 %)	
Distance to nearest major blue space (m)	1760.8 ± 1634.9	1864.9 ± 1411.6	<0.001
missing	547 (10.1 %)	334 (3.9 %)	
<b>Air pollution during pregnancy</b>			
NO <sub>2</sub> (µg/m <sup>3</sup> )	21.7 ± 10.3	21.8 ± 6.5	0.53
missing	499 (9.2 %)	385 (4.5 %)	
PM <sub>2.5</sub> (µg/m <sup>3</sup> )	15.3 ± 3.3	13.5 ± 3.4	<0.001
missing	65 (1.2 %)	122 (1.4 %)	
<b>Built environment during childhood</b>			
Population density (inhabitants/km <sup>2</sup> )	6336.7 ± 7721.2	4960.5 ± 3056.6	<0.001
missing	47 (0.9 %)	1142 (13.4 %)	
Building density (m <sup>2</sup> /km <sup>2</sup> )			
100-m buffer	236217.7 ± 147718.4	188261.8 ± 79105.3	<0.001
missing	578 (10.7 %)	2596 (30.4 %)	
300-m buffer	196928.8 ± 126199.1	164041.5 ± 71044.7	<0.001
missing	521 (9.6 %)	2465 (28.8 %)	
Facility density (facilities/km <sup>2</sup> , 300-m buffer)	35.7 ± 49.6	34.7 ± 44	0.238
missing	23 (0.4 %)	1030 (12 %)	
Facility richness (facility types/km <sup>2</sup> , 300-m buffer)	0.1 ± 0.1	0.1 ± 0.1	0.006
missing	23 (0.4 %)	1030 (12 %)	
Land use diversity (300-m buffer)	0.5 ± 0.1	0.5 ± 0.1	0.006
missing	1684 (31.2 %)	5383 (63 %)	
Connectivity density (intersections/km <sup>2</sup> )			
100-m buffer	224.3 ± 145.5	227.7 ± 145.7	0.205
missing	664 (12.3 %)	1716 (20.1 %)	
300-m buffer	174 ± 93.1	178.7 ± 86.8	0.006
missing	509 (9.4 %)	1590 (18.6 %)	
Density of public bus stops (stops/km <sup>2</sup> )			
100-m buffer	27.6 ± 80	25.5 ± 40.7	0.111
missing	1041 (19.3 %)	1933 (22.6 %)	

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	Mean ± sd or N (%) <sup>a</sup>		P-value
	Participants (N=5403)	Non-Participants (N=8551)	
<i>300-m buffer</i>	24.9 ± 35.1	24.8 ± 17.6	0.776
missing	1002 (18.5 %)	1923 (22.5 %)	
<i>500-m buffer</i>	21.8 ± 22.9	22.8 ± 11.5	0.006
missing	955 (17.7 %)	1917 (22.4 %)	
Walkability index (300-m buffer)	0.3 ± 0.1	0.3 ± 0.1	<0.001
missing	1932 (35.8 %)	5387 (63 %)	
Natural spaces during childhood			
NDVI			
<i>100-m buffer</i>	0.4 ± 0.1	0.4 ± 0.1	<0.001
missing	72 (1.3 %)	1362 (15.9 %)	
<i>300-m buffer</i>	0.4 ± 0.1	0.5 ± 0.1	<0.001
missing	72 (1.3 %)	1361 (15.9 %)	
<i>500-m buffer</i>	0.4 ± 0.1	0.5 ± 0.1	<0.001
missing	72 (1.3 %)	1361 (15.9 %)	
Distance to nearest major green space (m)	169.6 ± 155.9	178 ± 146.9	0.003
missing	610 (11.3 %)	1753 (20.5 %)	
Distance to nearest major blue space (m)	1772.1 ± 1634.4	1823 ± 1258.6	0.07
missing	610 (11.3 %)	1753 (20.5 %)	
Air pollution during childhood			
NO <sub>2</sub> (µg/m <sup>3</sup> )	25.1 ± 11.6	29 ± 7	<0.001
missing	38 (0.7 %)	6302 (73.7 %)	
PM <sub>2.5</sub> (µg/m <sup>3</sup> )	15.2 ± 2.7	13.8 ± 2.1	<0.001
missing	38 (0.7 %)	6302 (73.7 %)	
Parental characteristics			
Parents place of birth			
<i>None or one in the country of inclusion</i>	1707 (31.8 %)	4250 (50.2 %)	<0.001
<i>Both</i>	3654 (68.2 %)	4212 (49.8 %)	
missing	42 (0.8 %)	89 (1 %)	
Deprivation index at area-level during pregnancy			
<i>less deprived</i>	1397 (29.1 %)	1258 (15.9 %)	<0.001
<i>middle deprived</i>	1734 (36.2 %)	2816 (35.6 %)	
<i>most deprived</i>	1662 (34.7 %)	3846 (48.6 %)	
missing	610 (11.3 %)	631 (7.4 %)	
Deprivation index at area-level at four- to five years old			
<i>less deprived</i>	1521 (31.8 %)	1034 (16.4 %)	<0.001
<i>middle deprived</i>	1786 (37.3 %)	2320 (36.8 %)	
<i>most deprived</i>	1477 (30.9 %)	2956 (46.8 %)	
missing	619 (11.5 %)	2241 (26.2 %)	
Maternal age (years)	29.8 ± 5.2	28.2 ± 5.6	<0.001
missing	32 (0.6 %)	16 (0.2 %)	
Maternal educational level			
<i>less than primary, primary, and lower secondary</i>	1610 (31 %)	3689 (46.2 %)	<0.001
<i>upper secondary, and post-secondary non-tertiary</i>	1695 (32.7 %)	1865 (23.4 %)	
<i>tertiary</i>	1884 (36.3 %)	2425 (30.4 %)	
missing	214 (4 %)	572 (6.7 %)	
Maternal pre-pregnancy body mass index (kg/m <sup>2</sup> )	25.4 ± 5.4	27.3 ± 5.7	<0.001
missing	116 (2.1 %)	290 (3.4 %)	
Parity			
<i>no child</i>	2328 (44.2 %)	3813 (46 %)	<0.001
<i>1 child</i>	1802 (34.2 %)	2351 (28.4 %)	
<i>≥ 2 children</i>	1140 (21.6 %)	2119 (25.6 %)	
missing	133 (2.5 %) 268 (3.1 %)		
Maternal smoking during pregnancy			
<i>no</i>	4094 (78.3 %)	6450 (78.1 %)	0.762
<i>yes</i>	1133 (21.7 %)	1810 (21.9 %)	
missing	176 (3.3 %)	291 (3.4 %)	
Paternal age (years)	33.5 ± 5.3	32.5 ± 5.9	<0.001
missing	2193 (40.6 %)	6959 (81.4 %)	
Paternal educational level			
<i>less than primary, primary, and lower secondary</i>	1568 (33 %)	2963 (44.2 %)	<0.001
<i>upper secondary, and post-secondary non-tertiary</i>	1702 (35.9 %)	1558 (23.3 %)	
<i>tertiary</i>	1477 (31.1 %)	2176 (32.5 %)	
missing	656 (12.1 %)	1854 (21.7 %)	
Paternal body mass index			
<i>&lt;25 kg/m<sup>2</sup></i>	1280 (42 %)	759 (47.9 %)	0.001
<i>25-29 kg/m<sup>2</sup></i>	1354 (44.4 %)	627 (39.6 %)	
<i>≥ 30 kg/m<sup>2</sup></i>	413 (13.6 %)	199 (12.6 %)	
missing	2356 (43.6 %)	6966 (81.5 %)	
Child characteristics			
Season of birth			
<i>winter</i>	1316 (24.5 %)	2176 (25.5 %)	<0.001

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	Mean $\pm$ sd or N (%) <sup>a</sup>		P.value
	Participants (N=5403)	Non-Participants (N=8551)	
<i>spring</i>	1369 (25.5 %)	1877 (22 %)	
<i>summer</i>	1320 (24.5 %)	2190 (25.6 %)	
<i>autumn</i>	1374 (25.5 %)	2307 (27 %)	
missing	24 (0.4 %)	1 (0 %)	
Child sex			
<i>female</i>	2615 (48.4 %)	4164 (48.7 %)	0.756
<i>male</i>	2786 (51.6 %)	4386 (51.3 %)	
missing	2 (0 %)	1 (0 %)	

BiB, Born in Bradford; EDEN, Étude des Déterminants Pré et Postnatals du Développement et de la Santé de l'Enfant; INMA, Infancia y Medio Ambiente; NDVI, Normalized Difference Vegetation Index; NO<sub>2</sub>, nitrogen dioxide; PM<sub>2.5</sub>, particulate matter with an aerodynamic diameter of less than 2.5  $\mu$ m; RHEA, Mother-Child Cohort in Crete.

### 3 Cognitive and motor assessment

#### 3.1 British Picture Vocabulary Scale (BiB, UK)

Verbal abilities were assessed in children from the BiB cohort with the British Picture Vocabulary Scale (BPVS), a validated test assessing a child's oral language and receptive vocabulary.<sup>3</sup> The BPVS includes 14 sets, and each test contains 12 vocabulary questions. For each question, the assessor says a word and the child responds by selecting a picture from four options that best illustrates the word's meaning.

#### 3.2 Clinical Kinematic Assessment Tool (BiB, UK)

Fine motor ability was assessed in children from the BiB cohort with the Clinical-Kinematic Assessment Tool (CKAT), a validated sensorimotor test assessing manual visuomotor tracking, aiming and tracing performance.<sup>4</sup> The CKAT computerized tasks were presented on a tablet PC (screen = 260 x 163 mm). The screen was folded down horizontally to mimic a writing position, and children used a digital stylus in their preferred hand. The CKAT included 3 subtasks:

- Tracking: participants kept the stylus on a dot as it moved around the screen in a figure-of-eight. Dot speed increased from slow (4 s per figure-of-eight), to medium (8 s) to fast (16 s), with three repetitions at each speed (i.e., nine trials total).
- Aiming: participants made discrete movements between dots that appeared in a recurring shape of a pentagram. The five movements comprising the pentagram shape repeated 10 times.
- Steering: participants traced a path, keeping the stylus within a moving box that progressed every 5 s. Across six trials, the path shape became a mirror-image of itself on every other trial.

#### 3.3 Wechsler Preschool and Primary Scale of Intelligence (EDEN, France)

Children's cognitive function was assessed by trained psychologists (1 in each study center) with the French version of the Wechsler Preschool and Primary Scale of Intelligence Third Edition (WPPSI-III) in the EDEN cohort.<sup>5</sup> The WPPSI-III includes 14 subtests, designated as: core, supplemental, or optional. The core subtests of the battery were assessed to obtain composite scores for Verbal, and Performance IQ. Full scale IQ is calculated as the sum of Verbal, and Performance IQ.

- Verbal IQ
  - Information: for 6 Picture Items, the child responds to a question by choosing a picture from four response options. For 28 Verbal Items, the child answers questions that address a broad range of general knowledge topics.
  - Vocabulary: for 5 Picture Items, the child names pictures that are displayed in a stimulus book. For 25 Verbal Items, the child gives definitions for words that the examiner reads aloud.
  - Word reasoning: The child is read an increasingly specific series of one to three clues and identifies the common object or concept being described. This subtest is designed to measure fluid reasoning (inductive reasoning) ability. (28 items)
- Performance IQ
  - Block design: while viewing a constructed model or a picture in a stimulus book, the child uses one- or two-color blocks to re-create the design within a specified time limit. (20 items)
  - Matrix reasoning: the child looks at an incomplete matrix and selects the missing portion from 4 or 5 response options. (29 items)
  - Picture concepts: the child is presented with two or three rows of pictures and chooses one picture from each row to form a group with a common characteristic. (28 items)

Verbal IQ and Performance IQ subscales were used to assess verbal and non-verbal abilities, respectively.

#### 3.4 Peg Moving Task-5 (EDEN, France)

Children's fine motor function was evaluated by the Peg-moving task in the EDEN cohort.<sup>6</sup> After a demonstration by the examiner, children needed to move five pegs, one by one, to the hole in the opposite row. Each hand performed two trials, one trial from the nearest row to the farthest one and one trial from the farthest row to the nearest one. The task started with the preferred hand, then the participant needed to perform two trials with the non-preferred hand, and the task finished with a trial with the preferred hand. The peg-moving task was scored as the total time for the four trials for each hand.

#### 3.5 McCarthy Scales of Children's Abilities (INMA, Spain and RHEA, Greece)

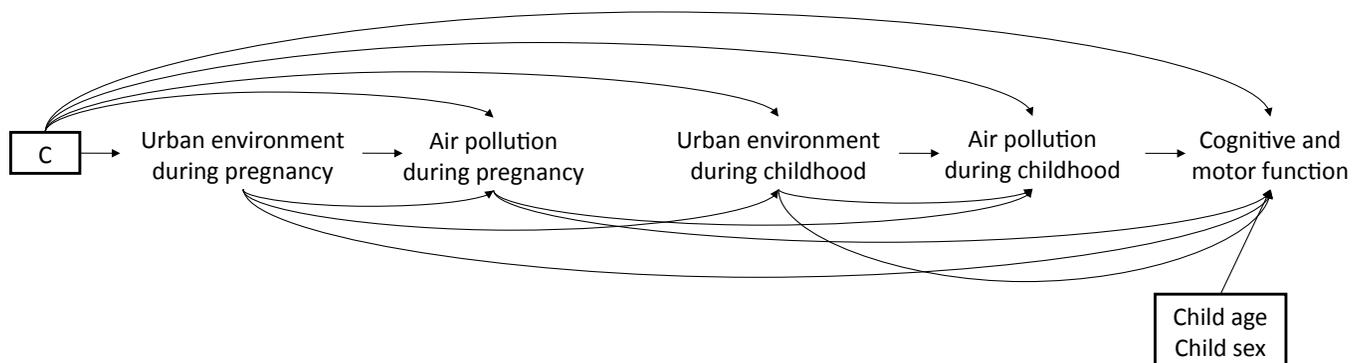
Cognitive and motor function was assessed by trained psychologists using the McCarthy Scales of Children's Abilities (MSCA)<sup>7</sup>, a validated tool for neuropsychological assessment in children aged 2.5-8.5 years old. The MSCA includes a general cognitive development score and 5 conventional sub-area scores. For this analysis we used sub-areas of 1) Verbal scale, which measures verbal expression and maturity of verbal concept; 2) Perceptual-performance, which measures reasoning ability through manipulation of materials; and 3) Motor scale, which measures both fine (i.e., drawing) and gross (i.e., playing with a ball) motor skills. Cognitive

and motor function was assessed using the Spanish version of the MSCA for children from the INMA cohort. All testing was done in the health care center by 5 specially trained psychologists. Cognitive and motor function was assessed by two trained psychologists at the University Hospital of Heraklion, Greece, using the Greek version of the MSCA for the RHEA cohort. Children were assigned to the two psychologists at random.

## 4 Statistical analyses

### 4.1 Directed Acyclic Graph

Figure S5: Directed Acyclic Graph



C: study area, parental education, parental BMI, parity, season of birth

### 4.2 Multiple imputation processing

Neuro-outcomes and an area indicator were forced in as predictors in the imputation models. We used variables as predictors when they were correlated with the exposure levels and/or with the probability of the exposure being missing (absolute correlation value  $>0.3$ ). We also ensured that for each predictor, the proportion of observed values among the non-observed values was greater than 50%. We restricted the number of predictors in the imputation models to fewer than 25 variables.<sup>8</sup> After imputation, we conducted the following diagnostics. We compared imputed and observed data using density plots and stripplots of van Buuren and Greenacre<sup>8</sup> These types of comparison were only done when there were more than 5% of non-observed values. Numerically, we checked that variables had 1) an absolute difference between means of the observed and imputed values smaller than 2 standard deviations; and 2) a ratio of variances of the observed and imputed values between 0.5 and 2. For categorical variables, we ensured the p-value of the chi-squared test between imputed and non-imputed values was  $>0.05$ .

### 4.3 Multi-exposure analysis (Deletion-Substitution-Addition algorithm)

The Deletion-Substitution-Addition algorithm is an iterative selection method, which selects the variables that are most predictive of the outcome by cross-validation, taking into account the correlation matrix of the variables, and simultaneously correcting for multiple testing. At each iteration, the algorithm allows three steps, namely: 1) deletion, removal of a variable; 2) substitution, replacement of one variable with another; and 3) addition, insertion of a variable to the model. The process to the optimal model (i.e. a combination of variables with the smallest value of root-mean-square deviation) starts with a model containing only the intercept, and continues with the deletion, substitution, and addition processes. To assure the adjustment for all potential confounding variables in each model, we fixed the potential confounding variables (including the area), allowing only the exposure variables to participate in the selection process. We applied DSA to the 20th imputed dataset.

## 5 Single-exposure associations

Table S8: Single-exposure associations between urban environment in early-life and cognitive and motor development

	IQR	Non-verbal abilities		Verbal abilities		Fine motor function		Gross motor function	
		Estimate (95%CI)	P.value	Estimate (95%CI)	P.value	Estimate (95%CI)	P.value	Estimate (95%CI)	P.value
Built environment during pregnancy									
Population density (inhabitants/km <sup>2</sup> )	7415	0.2 (-0.3, 0.8)	0.46	-0.2 (-0.7, 0.4)	0.54	-0.5 (-1.1, 0.1)	0.08	0.1 (-0.6, 0.7)	0.83
Building density (m <sup>2</sup> /km <sup>2</sup> )									
100-m buffer	162041	0.2 (-0.5, 0.8)	0.59	0.1 (-0.5, 0.7)	0.77	-0.2 (-0.8, 0.4)	0.53	0 (-0.7, 0.8)	0.92
300-m buffer	131637	0.2 (-0.4, 0.8)	0.43	-0.1 (-0.6, 0.4)	0.73	-0.1 (-0.7, 0.5)	0.73	0.1 (-0.6, 0.9)	0.73
Facility density (facilities/km <sup>2</sup> , 300-m buffer)	53.1	0.2 (-0.6, 0.9)	0.67	-0.3 (-0.9, 0.4)	0.40	-0.2 (-0.9, 0.5)	0.54	0.2 (-0.7, 1.2)	0.63
Facility richness (facility types/km <sup>2</sup> , 300-m buffer)	0.1	0.2 (-0.7, 1)	0.72	-0.1 (-0.8, 0.6)	0.71	-0.2 (-0.9, 0.4)	0.49	0.3 (-0.6, 1.3)	0.45
Land use diversity (300-m buffer)	0.1	-0.1 (-0.7, 0.6)	0.83	-0.9 (-1.5, -0.4)	<0.01	0.2 (-0.4, 0.8)	0.54	-0.1 (-0.9, 0.8)	0.83
Connectivity density (intersections/km <sup>2</sup> )									
100-m buffer	192.2	-0.1 (-0.8, 0.6)	0.79	-0.8 (-1.4, -0.3)	<0.01	0 (-0.6, 0.6)	0.88	0.8 (-0.2, 1.8)	0.10
300-m buffer	128.1	0.2 (-0.4, 0.9)	0.48	-0.2 (-0.8, 0.3)	0.41	0 (-0.5, 0.6)	0.89	0.4 (-0.4, 1.3)	0.32
Density of public bus stops (stops/km <sup>2</sup> )									
100-m buffer	32	0.1 (-1.1, 1.4)	0.83	-0.2 (-1.1, 0.6)	0.58	0.1 (-0.8, 1)	0.80	-0.2 (-1.7, 1.4)	0.84
300-m buffer	24.9	0 (-0.8, 0.8)	0.97	-0.1 (-0.8, 0.6)	0.82	-0.5 (-1.2, 0.3)	0.24	0 (-1, 0.9)	0.93
500-m buffer	20.5	0.4 (-0.5, 1.2)	0.39	-0.2 (-0.9, 0.5)	0.59	-0.3 (-1.1, 0.5)	0.44	0.2 (-0.7, 1.1)	0.69
Walkability index (300-m buffer)	0.1	0 (-0.8, 0.8)	0.99	-0.7 (-1.4, -0.1)	0.03	-0.1 (-0.8, 0.6)	0.85	0.3 (-0.7, 1.3)	0.57
Natural spaces during pregnancy									
NDVI									
100-m buffer	0.2	-1 (-2.3, 0.4)	0.15	0.9 (0, 1.9)	0.06	0 (-1.1, 1.1)	0.99	-0.1 (-2, 1.7)	0.89
300-m buffer	0.2	-0.9 (-2.2, 0.3)	0.14	1.1 (0.2, 2.1)	0.02	-0.1 (-1.2, 0.9)	0.79	-0.5 (-2.2, 1.2)	0.58
500-m buffer	0.2	-0.7 (-1.9, 0.5)	0.28	1.2 (0.2, 2.1)	0.02	-0.1 (-1.2, 1)	0.84	0 (-1.7, 1.7)	0.97
Distance to nearest major green space (m)	200.2	0.6 (-0.2, 1.3)	0.15	0.1 (-0.5, 0.7)	0.83	-0.3 (-1, 0.4)	0.38	-0.4 (-1.4, 0.6)	0.43
Distance to nearest major blue space (m)	1747.2	0 (-0.8, 0.7)	0.96	-0.1 (-0.7, 0.5)	0.66	0.1 (-0.5, 0.8)	0.70	0.1 (-0.8, 1)	0.84
Air pollution during pregnancy									
NO <sub>2</sub> (µg/m <sup>3</sup> )	9.6	0.1 (-0.6, 0.8)	0.77	-0.2 (-0.8, 0.5)	0.62	-0.7 (-1.4, 0.1)	0.07	0 (-0.8, 0.8)	0.98
PM <sub>2.5</sub> (µg/m <sup>3</sup> )	3.2	0.6 (-0.5, 1.7)	0.27	0.4 (-0.4, 1.1)	0.38	-1.2 (-2.1, -0.4)	<0.01	0.8 (-0.6, 2.3)	0.27
Built environment during childhood									
Population density (inhabitants/km <sup>2</sup> )	7766	0.2 (-0.5, 0.8)	0.59	-0.1 (-0.8, 0.5)	0.64	-0.3 (-1, 0.4)	0.36	-0.1 (-0.8, 0.7)	0.85
Building density (m <sup>2</sup> /km <sup>2</sup> )									
100-m buffer	158140	0 (-0.6, 0.7)	0.94	-0.1 (-0.7, 0.5)	0.66	-0.3 (-0.9, 0.3)	0.36	0.1 (-0.6, 0.9)	0.72
300-m buffer	133077	0.1 (-0.5, 0.7)	0.79	-0.2 (-0.8, 0.3)	0.41	-0.3 (-0.9, 0.3)	0.37	0.1 (-0.6, 0.8)	0.77
Facility density (facilities/km <sup>2</sup> , 300-m buffer)	46	0.4 (-0.5, 1.3)	0.40	-0.1 (-0.8, 0.6)	0.80	-0.3 (-1, 0.5)	0.51	0 (-1.1, 1)	0.93
Facility richness (facility types/km <sup>2</sup> , 300-m buffer)	0.1	0.4 (-0.4, 1.2)	0.30	0 (-0.6, 0.7)	0.95	-0.1 (-0.8, 0.6)	0.84	0.2 (-0.8, 1.1)	0.73

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	IQR	Non-verbal abilities		Verbal abilities		Fine motor function		Gross motor function	
		Estimate (95%CI)	Pvalue	Estimate (95%CI)	Pvalue	Estimate (95%CI)	Pvalue	Estimate (95%CI)	Pvalue
Land use diversity (300-m buffer)	0.1	0.2 (-0.5, 0.8)	0.61	-0.6 (-1.1, 0)	0.04	0.4 (-0.2, 1)	0.16	-0.1 (-1, 0.7)	0.78
Connectivity density (intersections/km <sup>2</sup> )									
100-m buffer	192.2	0.3 (-0.5, 1.1)	0.48	-0.6 (-1.2, 0)	0.06	-0.1 (-0.8, 0.6)	0.81	0.9 (-0.1, 1.9)	0.08
300-m buffer	124.6	0.2 (-0.5, 0.9)	0.59	-0.2 (-0.8, 0.4)	0.49	0 (-0.6, 0.6)	0.88	0.5 (-0.4, 1.3)	0.26
Density of public bus stops (stops/km <sup>2</sup> )									
100-m buffer	32	0.6 (-0.7, 1.8)	0.36	0.3 (-0.6, 1.2)	0.49	0 (-1, 0.9)	0.92	-0.4 (-1.9, 1.1)	0.58
300-m buffer	24.9	0.3 (-0.7, 1.3)	0.54	0.4 (-0.5, 1.2)	0.39	-0.5 (-1.4, 0.4)	0.29	-0.1 (-1.2, 1)	0.87
500-m buffer	21.8	0.5 (-0.5, 1.4)	0.33	0.1 (-0.8, 1)	0.88	-0.3 (-1.3, 0.7)	0.54	-0.1 (-1.3, 1)	0.83
Walkability index (300-m buffer)	0.1	0.2 (-0.5, 0.9)	0.61	-0.7 (-1.2, -0.1)	0.03	0.2 (-0.4, 0.9)	0.42	0.1 (-0.8, 0.9)	0.87
Natural spaces during childhood									
NDVI									
100-m buffer	0.2	-0.9 (-2.2, 0.4)	0.17	0.8 (-0.2, 1.8)	0.12	-0.2 (-1.2, 0.9)	0.77	-0.1 (-1.9, 1.7)	0.92
300-m buffer	0.2	-0.8 (-2, 0.5)	0.22	0.9 (-0.1, 1.9)	0.07	-0.2 (-1.3, 0.9)	0.69	-0.2 (-1.9, 1.4)	0.78
500-m buffer	0.2	-0.8 (-2, 0.5)	0.24	0.8 (-0.1, 1.8)	0.09	-0.4 (-1.5, 0.6)	0.42	0.3 (-1.4, 1.9)	0.73
Distance to nearest major green space (m)	182.4	0.2 (-0.6, 1)	0.61	-0.1 (-0.7, 0.5)	0.76	-0.2 (-0.9, 0.4)	0.50	-0.3 (-1.3, 0.6)	0.49
Distance to nearest major blue space (m)	1758.9	-0.1 (-0.8, 0.6)	0.80	-0.2 (-0.8, 0.4)	0.55	0.1 (-0.5, 0.8)	0.68	0.2 (-0.7, 1.1)	0.68
Air pollution during childhood									
NO2 (µg/m <sup>3</sup> )	17.5	0.5 (-0.6, 1.6)	0.35	-0.7 (-1.7, 0.3)	0.15	0.4 (-0.7, 1.5)	0.48	-0.7 (-1.9, 0.5)	0.25
PM2.5 (µg/m <sup>3</sup> )	3.2	0.9 (-0.3, 2)	0.13	-1.2 (-2.1, -0.4)	0.01	1 (0.1, 1.9)	0.04	0.7 (-0.6, 2)	0.28

CI, confidence interval; IQR, interquartile range; NDVI, Normalized Difference Vegetation Index; NO2, nitrogen dioxide; PM2.5, particulate matter with an aerodynamic diameter of less than 2.5 µm.

Estimates are expressed as mean change for an interquartile range increase of exposure. Estimates adjusted on area of inclusion, deprivation index at area level, season of birth, native parents of the country of recruitment, maternal and paternal age at recruitment, maternal smoking during pregnancy, maternal pre-pregnancy body mass index, paternal body mass index at recruitment, parity, maternal and paternal educational levels, child sex, and child age at assessment.

## 6 Multi-exposure associations

**Table S9: Multi-exposure associations between urban environment in early-life and cognitive and motor development (DSA selected models > 10%)**

	Pregnancy period		Childhood period	
		Estimate (95% CI)		Estimate (95% CI)
Verbal abilities (n = 5,363)				
Urban environment	<i>Model 1 (61%)<sup>a</sup></i>		<i>Model 1 (45%)<sup>a</sup></i>	
	Connectivity density in 100m buffer ( $\Delta$ 192.2 intersections/km <sup>2</sup> )	-0.8 (-1.4, -0.2)	Land use diversity ( $\Delta$ 0.1 units)	-0.6 (-1.1, 0.0)
	Land use diversity ( $\Delta$ 0.1 units)	-0.9 (-1.4, -0.3)		
	Building density in 100m buffer ( $\Delta$ 131,637 m <sup>2</sup> /km <sup>2</sup> )	0.8 (0.1, 1.5)	<i>Model 2 (32.5%)<sup>a</sup></i>	
	NDVI in 500m buffer ( $\Delta$ 0.2 units)	1.5 (0.4, 2.7)	Land use diversity ( $\Delta$ 0.1 units)	-0.6 (-1.1, 0.0)
			NDVI in 300m buffer ( $\Delta$ 0.2 units)	0.9 (-0.1, 1.9)
Air pollution	<i>Model 2 (38.5%)<sup>a</sup></i>		<i>Model 1 (98.5%)<sup>a</sup></i>	
	Connectivity density in 100m buffer ( $\Delta$ 192.2 intersections/km <sup>2</sup> )	-0.8 (-1.3, -0.2)	PM2.5 ( $\Delta$ 3.2 $\mu\text{g}/\text{m}^3$ )	-1.2 (-2.1, -0.4)
	Land use diversity ( $\Delta$ 0.1 units)	-0.9 (-1.4, -0.3)		
Fine motor function (n = 5,228)				
Air pollution	<i>Model 1 (93.5%)<sup>a</sup></i>		<i>Model 1 (45.5%)<sup>a</sup></i>	
	PM2.5 ( $\Delta$ 3.2 $\mu\text{g}/\text{m}^3$ )	-1.2 (-2.1, -0.4)	PM2.5 ( $\Delta$ 3.2 $\mu\text{g}/\text{m}^3$ )	1.0 (0.1, 1.9)

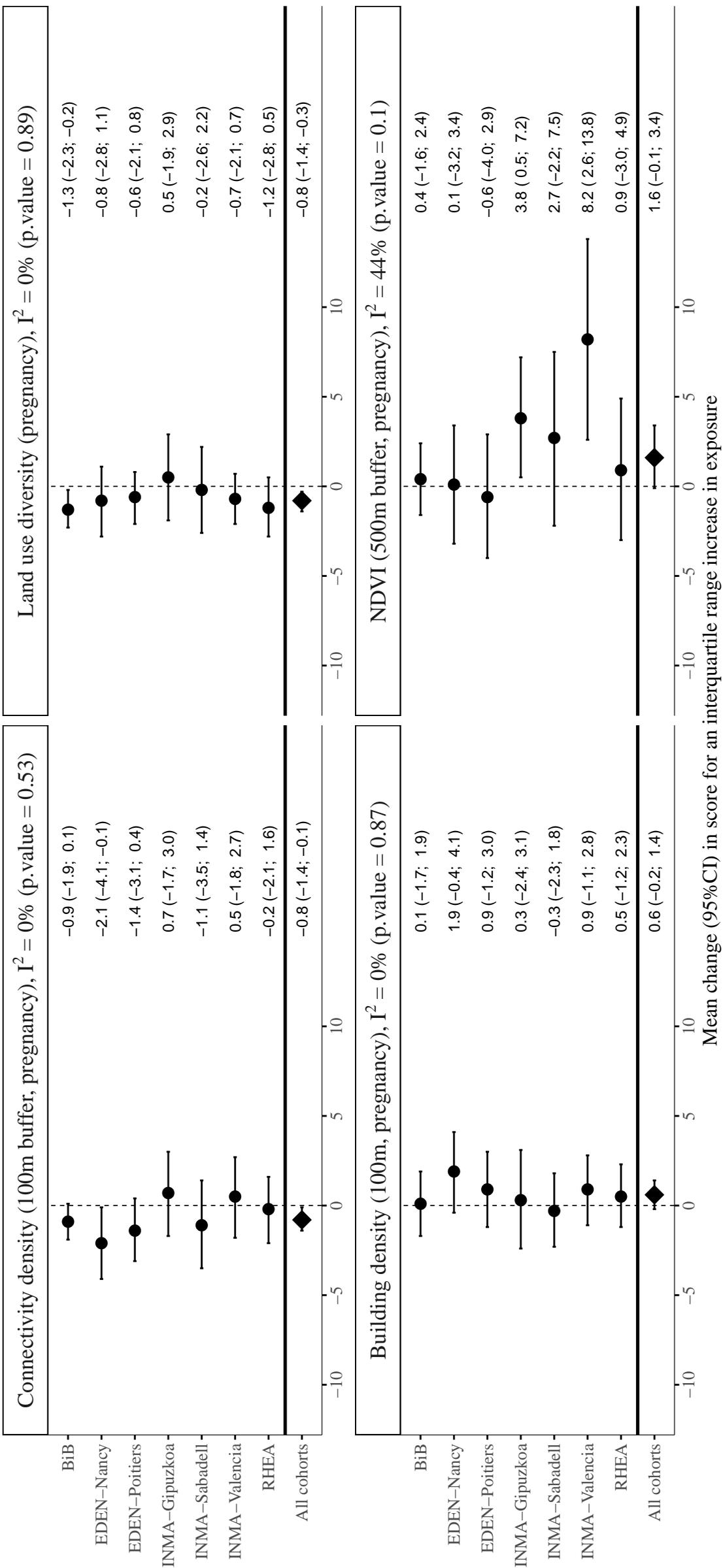
CI, confidence interval;  $\Delta$ , interquartile range increase; DSA, Deletion-Substitution-Addition algorithm; NDVI, Normalized Difference Vegetation Index; PM2.5, particulate matter with an aerodynamic diameter of less than 2.5  $\mu\text{m}$ .

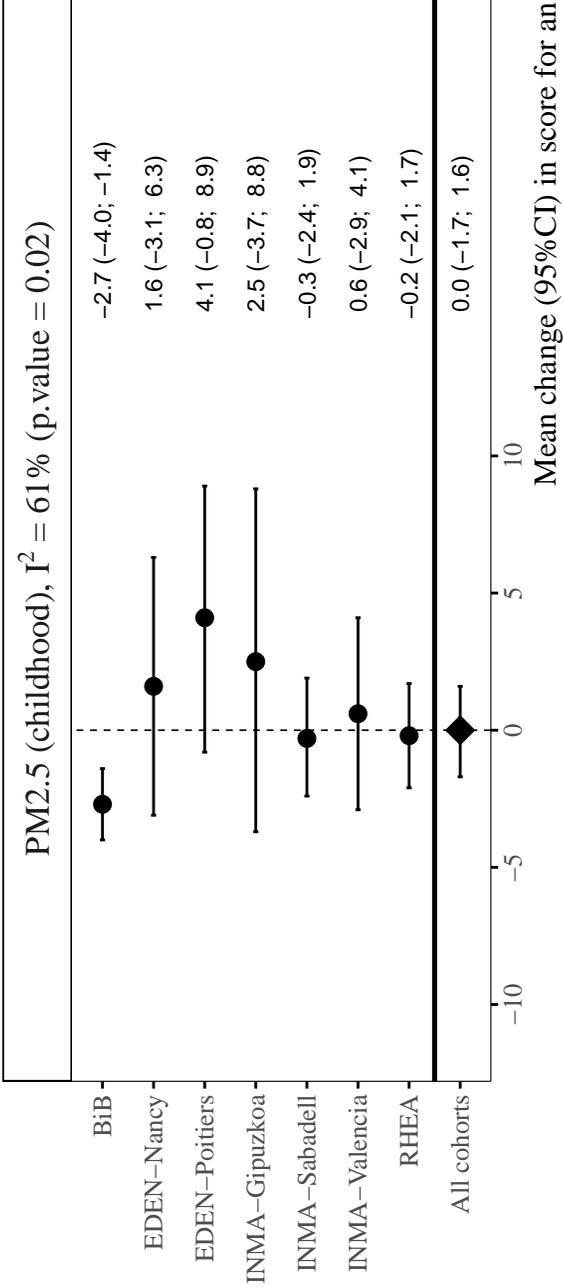
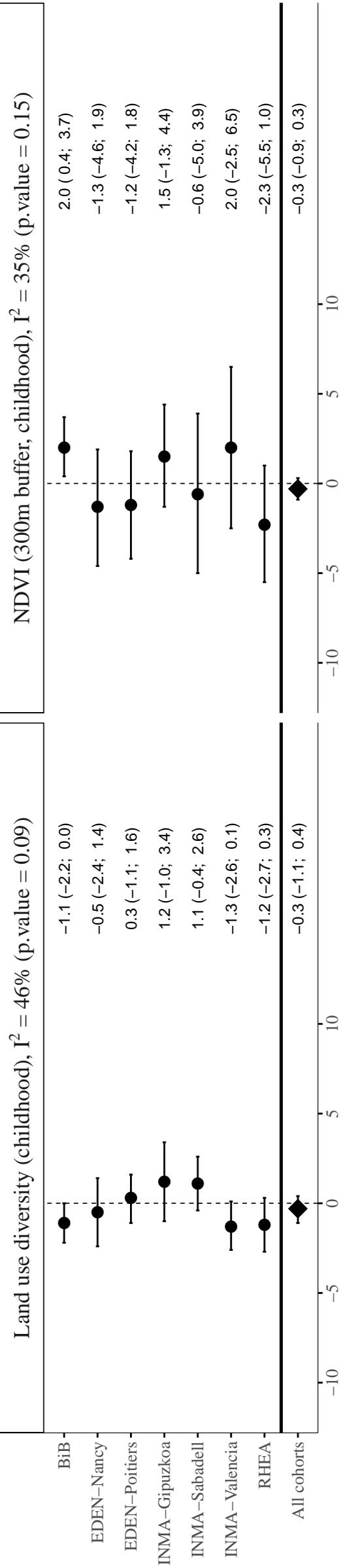
Estimates are expressed as mean change for an interquartile range increase of exposure. Estimates adjusted on co-exposures (urban environment or air pollution), area of inclusion, deprivation index at area level, season of birth, native parents of the country of recruitment, maternal and paternal age at recruitment, maternal smoking during pregnancy, maternal pre-pregnancy body mass index, paternal body mass index at recruitment, parity, maternal and paternal educational levels, child sex, and child age at assessment.

<sup>a</sup> Frequency of selection by DSA.

## 7 Meta-analyses stratified by cohort

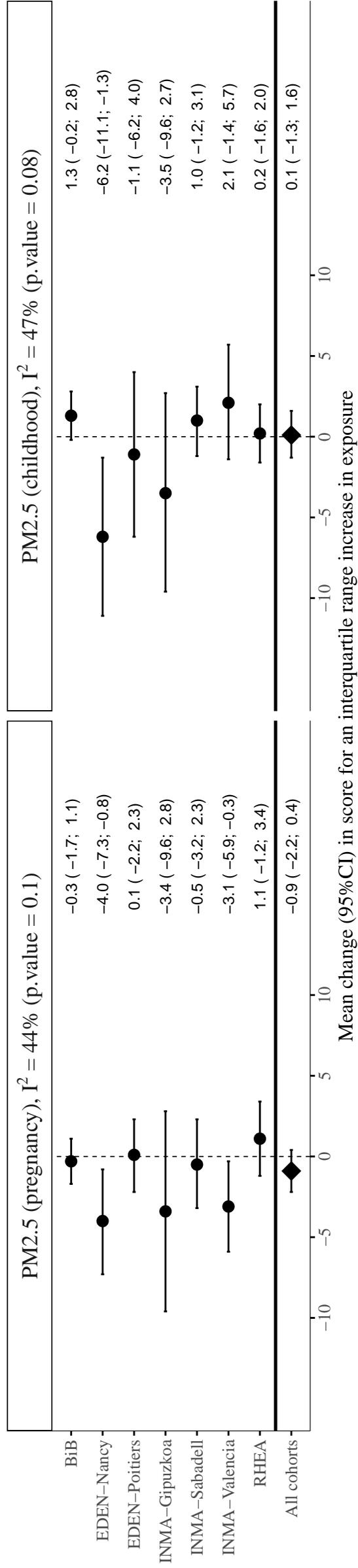
Figure S6: Associations with verbal abilities stratified by area using linear mixed-effect models (Der Simonian-Laird estimator)





BiB, Born in Bradford; CI, Confidence interval; EDEN, Étude des Déterminants Pré et Postnatals du Développement et de la Santé de l'Enfant; INMA, Infancia y Medio Ambiente; PM2.5, particulate matter with an aerodynamic diameter of less than 2.5  $\mu\text{m}$ ; RHEA, Mother-Child Cohort in Crete. Estimates are expressed as mean change for an interquartile range increase of exposure. Estimates adjusted on co-exposures (urban environment or air pollution), area of inclusion, deprivation index at area level, season of birth, native parents of the country of recruitment, maternal and paternal age at recruitment, maternal smoking during pregnancy, maternal pre-pregnancy body mass index, paternal body mass index at recruitment, parity, maternal and paternal educational levels, child sex, and child age at assessment.

Figure S7: Associations with fine motor function stratified by area using linear mixed-effect models (Der Simonian-Laird estimator)



BiB, Born in Bradford; CI, Confidence interval; EDEN, Étude des Déterminants Pré et Postnataux du Développement et de la Santé de l'Enfant; INMA, Infancia y Medio Ambiente; PM2.5, particulate matter with an aerodynamic diameter of less than 2.5  $\mu\text{m}$ ; RHEA, Mother-Child Cohort in Crete. Estimates are expressed as mean change for an interquartile range increase of exposure. Estimates adjusted on co-exposures (urban environment or air pollution), area of inclusion, deprivation index at area level, season of birth, native parents of the country of recruitment, maternal and paternal age at recruitment, maternal pre-pregnancy body mass index, paternal body mass index at recruitment, parity, maternal and paternal educational levels, child sex, and child age at assessment.

## References

- [1] HEREWeGo. HERE WeGo. URL <https://wego.here.com/>. accessed March 11, 2021.
- [2] European Environment Agency. Copernicus land monitoring service - urban atlas — european environment agency. URL <https://www.eea.europa.eu/data-and-maps/data/copernicus-land-monitoring-service-urban-atlas>. accessed March 3, 2021.
- [3] Dunn LM, Dunn LM, and Whetton C. *The British Picture Vocabulary Scale: manual for the short and long forms*. NFER-Nelson;1982. ISBN 978-0-7005-0495-4.
- [4] Culmer PR, Levesley MC, Mon-Williams M, and Williams JHG. A new tool for assessing human movement: The kinematic assessment tool. *Journal of Neuroscience Methods* 2009;**184**(1):184—192. ISSN 01650270. doi: 10.1016/j.jneumeth.2009.07.025.
- [5] Freeman S. *Wechsler Preschool and Primary Scale of Intelligence*;page 3351—3360. Springer;2013. ISBN 978-1-4419-1698-3.
- [6] Birkett P. Left, right, hand and brain: The right shift theory. *Biological Psychology* 1987;**25**:96—98. doi: 10.1016/0301-0511(87)90090-1.
- [7] Schrader A and D’Amato RC. *McCarthy Scales of Children’s Abilities*;page 1531 —1532. Springer;2011. ISBN 978-0-387-79948-3. doi: 10.1007/978-0-387-79948-3\_1462.
- [8] van Buuren S and Greenacre M. *Flexible Imputation of Missing Data*. Chapman & Hall/CRC Interdisciplinary Statistics;second edition;2018. ISBN 978-0-429-49225-9.