

Note to readers with disabilities: *EHP* strives to ensure that all journal content is accessible to all readers. However, some figures and Supplemental Material published in *EHP* articles may not conform to [508 standards](#) due to the complexity of the information being presented. If you need assistance accessing journal content, please contact ehp508@niehs.nih.gov. Our staff will work with you to assess and meet your accessibility needs within 3 working days.

Supplemental Material

Exposure to Air Pollution during Pregnancy and Childhood, and White Matter Microstructure in Preadolescents

Małgorzata J. Lubczyńska, Ryan L. Muetzel, Hanan El Marroun, Xavier Basagaña, Maciej Strak, William Denault, Vincent W.V. Jaddoe, Manon Hillegers, Meike W. Vernooij, Gerard Hoek, Tonya White, Bert Brunekreef, Henning Tiemeier, and Mònica Guxens

Table of Contents

Table S1. Table illustrating the details of the imputation modeling.

Figure S1. Description of the obtained inverse probability weights (IPW).

Table S2. LUR R^2 and R^2 cross validation.

Table S3. Exposure levels to NO_x and NO_2 during pregnancy by participant characteristics.

Table S4. Exposure levels to PM_{10} and $\text{PM}_{\text{coarse}}$ during pregnancy by participant characteristics.

Table S5. Exposure levels to $\text{PM}_{2.5}$ and $\text{PM}_{2.5\text{abs}}$ during pregnancy by participant characteristics.

Table S6. Exposure levels to PAHs and B[a]P during pregnancy by participant characteristics.

Table S7. Exposure levels to OC and Cu during pregnancy by participant characteristics.

Table S8. Exposure levels to Fe and K during pregnancy by participant characteristics.

Table S9. Exposure levels to Si and Zn during fetal life by participant characteristics.

Table S10. Exposure levels to OP_{DTT} and OP_{ESR} during pregnancy by participant characteristics.

Table S11. Exposure levels to UFP during pregnancy by participant characteristics.

Figure S2. Correlations between levels of the pollutants during pregnancy.

Figure S3. Correlations between levels of the pollutants during childhood.

Table S12. Results of multi-pollutant models selected by the Deletion/Substitution/Addition algorithm for pregnancy exposures in relation to global fractional anisotropy and global mean diffusivity, respectively, excluding participants of mothers recruited after birth (n=310).

Table S13. Results of analyses in which pregnancy and childhood exposures that were selected by Deletion/Substitution/Addition algorithm, and were nominally significant in the single pollutant models, were introduced simultaneously in the model in relation to global fractional anisotropy and global mean diffusivity, respectively.

Table S14. Adjusted linear regression analyses of fractional anisotropy in twelve individual white matter tracts in relation to pregnancy PM_{2.5}, and childhood NO_x exposures.

Table S15. Adjusted linear regression analyses of mean diffusivity in twelve individual white matter tracts in relation to pregnancy Si, and childhood Zn and OP_{DTT} exposures.

Table S16. Results of analyses in which pregnancy and childhood exposures selected by Deletion/Substitution/Addition algorithm were introduced simultaneously in the model in relation to global mean diffusivity in three white matter tracts.

Table S17. Results of the adjusted associations between exposure during pregnancy and childhood to single air pollutants and global fractional anisotropy, and global mean diffusivity at 9-12y, with and without accounting for measurement error.

Table S1: Table illustrating the details of the imputation modeling

Software used and key settings:
STATA 14.0 software (Stata Corporation, College Station, Texas) – Ice command (with 10 cycles)
Number of imputed datasets created:
25
Variables included in the imputation procedure:
global fractional anisotropy, global mean diffusivity, global axial diffusivity, and global radial diffusivity; concentration levels of the pollutants during pregnancy and childhood; maternal and paternal education, country of birth, age, height, weight, and psychological distress during pregnancy; maternal smoking and alcohol consumption during pregnancy, gestational age, parity, marital status, intelligence quotient, and household income; and child's ethnicity, genetic ancestry (10 principal components), gender, and age at the scanning session.
Treatment of binary/categorical variables:
logistic and multinomial models
Statistical interactions included in imputation models:
none

Figure S1: Description of the obtained inverse probability weights (IPW)

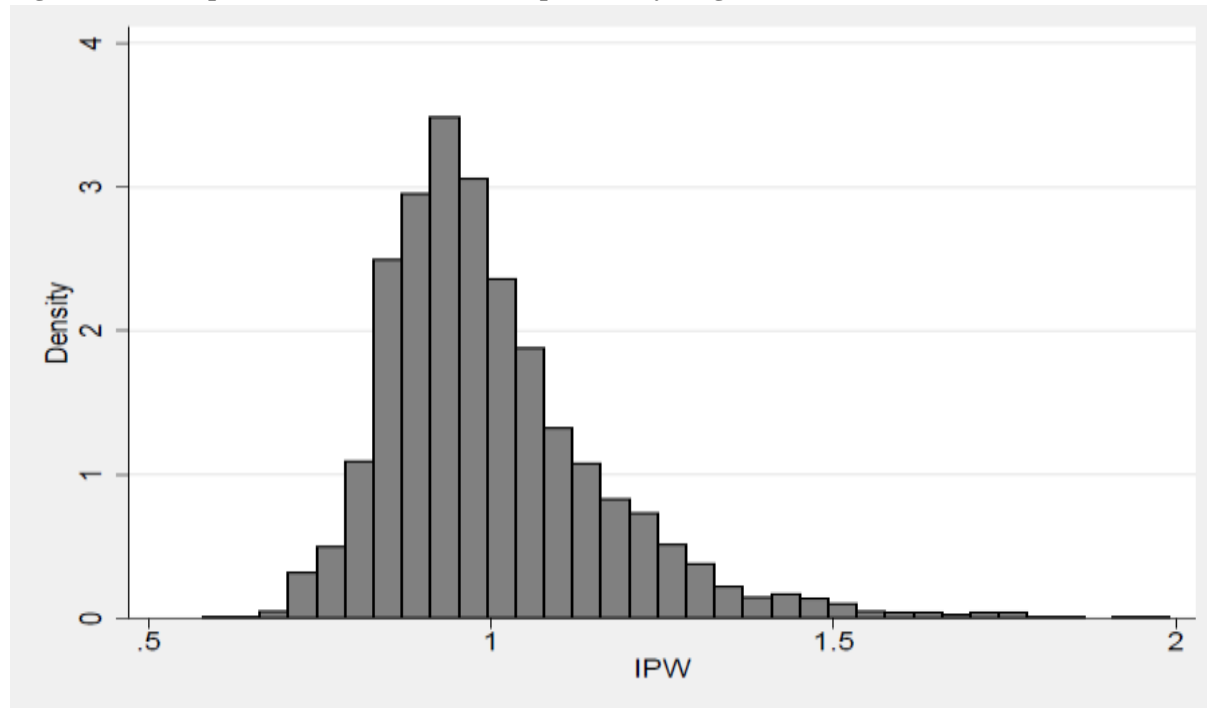


Figure S1: Distribution of the final inverse probability weights. The predictors used for the initial calculation of the weights were parental age, participation of the partner in the study, parental ethnicity, child's ethnicity, parental education, marital status, household income, intake period (prenatal vs. postnatal), parity, maternal weight, parental body mass index, maternal height, maternal smoking during pregnancy, maternal alcohol consumption during pregnancy gestational birth weight, parental psychological distress, maternal intelligence quotient, child's gender, and child's genetic ancestry. The variables selected ($p < 0.2$) were maternal age, participation of the partner in the study, parental ethnicity, child's ethnicity, parental education, intake period (prenatal vs. postnatal), parity, maternal weight, maternal smoking during pregnancy, maternal intelligence quotient, child's gender, and child's genetic ancestry. Then, to reduce the influence of extreme values, we used the most significant variables ($p < 0.001$), i.e. maternal age, maternal education, parity, maternal weight, maternal smoking during pregnancy, maternal IQ, and child's genetic ancestry, to calculate the final weights.

Table S2: LUR R² and R² cross validation

LUR model	R ²	R ² CV
NO _X	87	82
NO ₂	86	81
PM ₁₀	68	60
PMcoarse	51	38
PM _{2.5}	67	61
PM _{2.5} abs	92	89
PAHs	58	31
B[a]P	64	39
OC	80	71
Cu	83	81
Fe	78	73
K	31	25
Si	46	39
Zn	66	58
OP _{DTT}	60	47
OP _{ESR}	67	60
UFP	42	20

Abbreviations: LUR, land use regression; CV, cross validation; NO_X, nitrogen oxides; NO₂, nitrogen dioxide; PM, particulate matter with different aerodynamic diameters: less than 10µm (PM₁₀); between 10µm and 2.5µm (PMcoarse); less than 2.5µm (PM_{2.5}); PM_{2.5}absorbance, absorbance of PM_{2.5} filters; PAHs, polycyclic aromatic hydrocarbons; B[a]P, benzo[a]pyrene; OC, organic carbon; OP, oxidative potential (evaluated using two acellular methods: OP_{DTT} – dithiothreitol and OP_{ESR} – electron spin resonance); UFP, ultra-fine particles. Source: NO_X and NO₂: Beelen et al. 2013; PM₁₀, PM_{2.5}, PM_{2.5}abs: Eeftens et al. 2012; PM_{2.5} composition: de Hoogh et al. 2013; OP: Yand et al. 2015; OC and PAHs: Jedynska et al. 2014; UFP: Montagne et al. 2015.

Table S3. Exposure levels to NO_x and NO₂ during pregnancy by participant characteristics

Participant characteristics	n	NO _x	p-value	NO ₂	p-value
Maternal education level			<.001		0.001
Primary education or lower	176	47.6 (10.6)		33.9 (3.9)	
Secondary education	1,092	50.7 (15.5)		34.5 (5.2)	
Higher education	1,453	52.2 (15.0)		35.0 (4.9)	
Paternal education level			0.4		0.2
Primary education or lower	92	50.2 (16.5)		34.2 (5.5)	
Secondary education	700	52.4 (16.6)		34.8 (5.7)	
Higher education	1,069	52.0 (14.9)		35.1 (4.8)	
Monthly household income at intake			<.001		0.002
<900€	172	47.8 (12.7)		33.8 (4.5)	
900€ - 1,600€	319	48.9 (13.6)		34.3 (4.3)	
1,600€ - 2,200€	329	53.6 (15.6)		35.2 (4.7)	
>2,200€	1,486	52.2 (15.5)		35.0 (5.2)	
Maternal country of birth			<.001		0.6
The Netherlands	1,702	51.9 (15.6)		34.7 (5.1)	
Other Western	252	52.0 (15.6)		34.9 (4.8)	
Non-Western	944	49.6 (13.3)		34.6 (4.6)	
Paternal country of birth			0.003		0.017
The Netherlands	1,419	52.6 (15.9)		35.0 (5.2)	
Other Western	120	52.8 (15.9)		35.7 (6.2)	
Non-Western	502	49.9 (13.9)		34.4 (4.7)	
Family status at intake			<.001		<.001
Married	1,394	50.4 (14.6)		34.4 (4.7)	
Living together	1,023	52.9 (15.8)		35.2 (5.3)	
No partner	292	49.0 (13.1)		34.6 (5.0)	
Maternal parity			<.001		<.001
nulliparous	1,630	52.4 (15.4)		35.2 (5.2)	
1 child	883	49.8 (14.2)		34.2 (4.4)	
2 or more children	338	49.1 (13.2)		34.0 (4.2)	
Maternal smoking use during pregnancy			0.5		0.9
Never	2,004	51.3 (14.9)		34.7 (5.0)	
Smoking use until pregnancy known	222	50.2 (14.2)		34.9 (5.2)	
Continued smoking use during pregnancy	338	51.5 (16.1)		34.7 (5.0)	
Maternal alcohol use during pregnancy			0.041		0.004
Never	973	50.5 (14.7)		34.4 (4.8)	
Alcohol use until pregnancy known	335	52.7 (16.0)		35.4 (5.6)	
Continued alcohol use during pregnancy	1,023	51.7 (14.9)		34.9 (4.9)	
Maternal age at intake (years)	2,954	0.05	0.007	0.04	0.015
Paternal age at intake (years)	2,077	0.00	0.9	0.01	0.6
Maternal pre-pregnancy body mass index (kg/m ²)	2,181	-0.02	0.4	-0.02	0.4
Paternal body mass index (kg/m ²)	2,070	-0.04	0.042	-0.05	0.013
Maternal height (cm)	2,638	0.06	0.002	0.03	0.2
Paternal height (cm)	2,074	0.06	0.010	0.01	0.5
Maternal psychological distress during pregnancy	2,237	0.01	0.7	0.04	0.1
Paternal psychological distress during pregnancy	1,785	-0.05	0.036	-0.01	0.7
Maternal intelligence quotient score	2,688	0.05	0.009	0.03	0.1

Abbreviations: NO_x, nitrogen oxide; NO₂, nitrogen dioxide.

Values are mean (standard deviation) per category using one-way ANOVA test for categorical variables, and are pairwise correlation coefficients for continuous variables

Table S4. Exposure levels to PM₁₀ and PMcoarse during pregnancy by participant characteristics

Participant characteristics	n	PM ₁₀	p-value	PMcoarse	p-value
Maternal education level			<.001		0.036
Primary education or lower	176	26.7 (1.1)		10.1 (0.9)	
Secondary education	1,092	27.0 (1.7)		9.9 (1.0)	
Higher education	1,453	27.3 (1.7)		9.9 (1.1)	
Paternal education level			0.040		0.9
Primary education or lower	92	26.9 (1.7)		9.9 (1.0)	
Secondary education	700	27.2 (1.9)		9.9 (1.1)	
Higher education	1,069	27.3 (1.7)		9.9 (1.1)	
Monthly household income at intake			<.001		0.001
<900€	172	26.8 (1.4)		10.0 (0.9)	
900€ - 1,600€	319	26.9 (1.5)		10.1 (0.9)	
1,600€ - 2,200€	329	27.4 (1.7)		10.1 (1.1)	
>2,200€	1,486	27.3 (1.7)		9.9 (1.1)	
Maternal country of birth			<.001		<.001
The Netherlands	1,702	27.3 (1.7)		9.8 (1.1)	
Other Western	252	27.2 (1.7)		9.9 (1.1)	
Non-Western	944	27.0 (1.4)		10.1 (0.9)	
Paternal country of birth			0.001		0.010
The Netherlands	1,419	27.3 (1.8)		9.9 (1.1)	
Other Western	120	27.3 (1.7)		10.1 (1.2)	
Non-Western	502	27.0 (1.5)		10.0 (0.9)	
Family status at intake			<.001		<.001
Married	1,394	27.1 (1.6)		9.8 (1.1)	
Living together	1,023	27.4 (1.8)		10.0 (1.1)	
No partner	292	26.9 (1.4)		10.0 (0.9)	
Maternal parity			<.001		<.001
nulliparous	1,630	27.3 (1.7)		10.0 (1.1)	
1 child	883	27.0 (1.6)		9.8 (1.0)	
2 or more children	338	27.0 (1.4)		9.9 (1.0)	
Maternal smoking use during pregnancy			0.8		0.1
Never	2,004	27.2 (1.6)		9.9 (1.1)	
Smoking use until pregnancy known	222	27.1 (1.6)		9.8 (1.1)	
Continued smoking use during pregnancy	338	27.2 (1.8)		10.0 (1.0)	
Maternal alcohol use during pregnancy			<.001		0.9
Never	973	27.0 (1.5)		9.9 (1.0)	
Alcohol use until pregnancy known	335	27.4 (1.8)		9.9 (1.1)	
Continued alcohol use during pregnancy	1,023	27.3 (1.7)		9.9 (1.1)	
Maternal age at intake (years)	2,954	0.06	<.001	-0.03	0.022
Paternal age at intake (years)	2,077	0.03	0.2	-0.04	0.1
Maternal pre-pregnancy body mass index (kg/m ²)	2,181	-0.03	0.2	0.01	0.5
Paternal body mass index (kg/m ²)	2,070	-0.03	0.2	-0.08	<.001
Maternal height (cm)	2,638	0.07	0.001	-0.06	0.003
Paternal height (cm)	2,074	0.08	<.001	-0.05	0.039
Maternal psychological distress during pregnancy	2,237	-0.02	0.4	0.07	0.001
Paternal psychological distress during pregnancy	1,785	-0.05	0.025	0.03	0.2
Maternal intelligence quotient score	2,688	0.09	<.001	-0.04	0.025

Abbreviations: PM, particulate matter with aerodynamic diameters of less than 10µm (PM₁₀); between 10µm and 2.5µm (PMcoarse).

Values are mean (standard deviation) per category using one-way ANOVA test for categorical variables, and are pairwise correlation coefficients for continuous variables

Table S5. Exposure levels to PM_{2.5} and PM_{2.5}abs during pregnancy by participant characteristics

Participant characteristics	n	PM _{2.5}	p-value	PM _{2.5} abs	p-value
Maternal education level			<.001		<.001
Primary education or lower	176	16.8 (0.4)		1.6 (0.2)	
Secondary education	1,092	17.0 (0.6)		1.6 (0.3)	
Higher education	1,453	17.0 (0.6)		1.7 (0.3)	
Paternal education level			0.2		0.3
Primary education or lower	92	16.9 (0.6)		1.6 (0.4)	
Secondary education	700	17.0 (0.7)		1.7 (0.3)	
Higher education	1,069	17.0 (0.6)		1.7 (0.3)	
Monthly household income at intake			<.001		<.001
<900€	172	16.9 (0.5)		1.6 (0.3)	
900€ - 1,600€	319	16.9 (0.6)		1.6 (0.3)	
1,600€ - 2,200€	329	17.1 (0.6)		1.7 (0.3)	
>2,200€	1,486	17.0 (0.7)		1.7 (0.3)	
Maternal country of birth			<.001		<.001
The Netherlands	1,702	17.0 (0.7)		1.7 (0.3)	
Other Western	252	17.0 (0.6)		1.7 (0.3)	
Non-Western	944	16.9 (0.5)		1.6 (0.3)	
Paternal country of birth			<.001		0.001
The Netherlands	1,419	17.1 (0.7)		1.7 (0.3)	
Other Western	120	17.0 (0.7)		1.7 (0.4)	
Non-Western	502	16.9 (0.5)		1.6 (0.3)	
Family status at intake			<.001		<.001
Married	1,394	17.0 (0.6)		1.6 (0.3)	
Living together	1,023	17.1 (0.7)		1.7 (0.3)	
No partner	292	16.9 (0.5)		1.6 (0.3)	
Maternal parity			<.001		<.001
nulliparous	1,630	17.0 (0.7)		1.7 (0.3)	
1 child	883	16.9 (0.6)		1.6 (0.3)	
2 or more children	338	16.9 (0.5)		1.6 (0.2)	
Maternal smoking use during pregnancy			0.4		1.0
Never	2,004	17.0 (0.6)		1.7 (0.3)	
Smoking use until pregnancy known	222	16.9 (0.6)		1.7 (0.3)	
Continued smoking use during pregnancy	338	17.0 (0.7)		1.7 (0.3)	
Maternal alcohol use during pregnancy			<.001		<.001
Never	973	16.9 (0.6)		1.6 (0.3)	
Alcohol use until pregnancy known	335	17.1 (0.7)		1.7 (0.3)	
Continued alcohol use during pregnancy	1,023	17.0 (0.7)		1.7 (0.3)	
Maternal age at intake (years)	2,954	0.03	0.12	0.05	0.007
Paternal age at intake (years)	2,077	0.00	0.9	0.02	0.3
Maternal pre-pregnancy body mass index (kg/m ²)	2,181	-0.02	0.3	-0.04	0.1
Paternal body mass index (kg/m ²)	2,070	-0.05	0.015	-0.03	0.1
Maternal height (cm)	2,638	0.07	<.001	0.07	0.001
Paternal height (cm)	2,074	0.07	0.001	0.06	0.011
Maternal psychological distress during pregnancy	2,237	-0.01	0.5	0.01	0.8
Paternal psychological distress during pregnancy	1,785	-0.04	0.1	-0.04	0.1
Maternal intelligence quotient score	2,688	0.08	<.001	0.07	<.001

Abbreviations: PM, particulate matter with aerodynamic diameters of less than 2.5µm (PM_{2.5}); PM_{2.5}abs, absorbance of PM_{2.5} filters. Values are mean (standard deviation) per category using one-way ANOVA test for categorical variables, and are pairwise correlation coefficients for continuous variables

Table S6. Exposure levels to PAHs and B[a]P during pregnancy by participant characteristics

Participant characteristics	n	PAHs	p-value	B[a]P	p-value
Maternal education level			0.3		0.7
Primary education or lower	176	1.0 (0.2)		0.1 (0.0)	
Secondary education	1,092	1.0 (0.3)		0.1 (0.0)	
Higher education	1,453	1.0 (0.3)		0.1 (0.0)	
Paternal education level			0.5		0.8
Primary education or lower	92	1.0 (0.3)		0.1 (0.0)	
Secondary education	700	1.0 (0.4)		0.1 (0.0)	
Higher education	1,069	1.0 (0.4)		0.1 (0.0)	
Monthly household income at intake			<.001		0.025
<900€	172	1.0 (0.3)		0.1 (0.0)	
900€ - 1,600€	319	1.0 (0.3)		0.1 (0.0)	
1,600€ - 2,200€	329	1.0 (0.3)		0.1 (0.0)	
>2,200€	1,486	0.9 (0.4)		0.1 (0.0)	
Maternal country of birth			0.001		0.1
The Netherlands	1,702	1.0 (0.3)		0.1 (0.0)	
Other Western	252	0.9 (0.3)		0.1 (0.0)	
Non-Western	944	1.0 (0.3)		0.1 (0.0)	
Paternal country of birth			0.048		0.4
The Netherlands	1,419	1.0 (0.4)		0.1 (0.0)	
Other Western	120	1.0 (0.4)		0.1 (0.0)	
Non-Western	502	1.0 (0.3)		0.1 (0.0)	
Family status at intake			<.001		0.001
Married	1,394	0.9 (0.3)		0.1 (0.0)	
Living together	1,023	1.0 (0.4)		0.1 (0.0)	
No partner	292	1.0 (0.3)		0.1 (0.0)	
Maternal parity			<.001		<.001
nulliparous	1,630	1.0 (0.4)		0.1 (0.0)	
1 child	883	0.9 (0.3)		0.1 (0.0)	
2 or more children	338	0.9 (0.3)		0.1 (0.0)	
Maternal smoking use during pregnancy			0.031		0.1
Never	2,004	1.0 (0.3)		0.1 (0.0)	
Smoking use until pregnancy known	222	0.9 (0.3)		0.1 (0.0)	
Continued smoking use during pregnancy	338	1.0 (0.4)		0.1 (0.0)	
Maternal alcohol use during pregnancy			0.7		0.5
Never	973	1.0 (0.3)		0.1 (0.0)	
Alcohol use until pregnancy known	335	1.0 (0.4)		0.1 (0.0)	
Continued alcohol use during pregnancy	1,023	1.0 (0.4)		0.1 (0.0)	
Maternal age at intake (years)	2,954	-0.11	<.001	-0.08	<.001
Paternal age at intake (years)	2,077	-0.07	0.003	-0.05	0.013
Maternal pre-pregnancy body mass index (kg/m ²)	2,181	0.01	0.7	-0.00	0.9
Paternal body mass index (kg/m ²)	2,070	-0.02	0.3	-0.02	0.3
Maternal height (cm)	2,638	-0.02	0.2	-0.00	0.9
Paternal height (cm)	2,074	-0.03	0.2	-0.00	0.7
Maternal psychological distress during pregnancy	2,237	0.05	0.020	0.04	0.1
Paternal psychological distress during pregnancy	1,785	0.03	0.2	0.02	0.5
Maternal intelligence quotient score	2,688	-0.03	0.2	-0.00	0.8

Abbreviations: PAHs, polycyclic aromatic hydrocarbons; B[a]P, benzo[a]pyrene.

Values are mean (standard deviation) per category using one-way ANOVA test for categorical variables, and are pairwise correlation coefficients for continuous variables

Table S7. Exposure levels to OC and Cu during pregnancy by participant characteristics

Participant characteristics	n	OC	p-value	Cu	p-value
Maternal education level			0.018		<.001
Primary education or lower	176	1.8 (0.3)		4.7 (0.5)	
Secondary education	1,092	1.7 (0.4)		4.8 (0.9)	
Higher education	1,453	1.7 (0.4)		4.9 (0.9)	
Paternal education level			0.6		0.033
Primary education or lower	92	1.8 (0.4)		4.9 (1.0)	
Secondary education	700	1.7 (0.4)		4.8 (0.9)	
Higher education	1,069	1.7 (0.4)		5.0 (0.9)	
Monthly household income at intake			<.001		0.5
<900€	172	1.8 (0.3)		4.8 (0.8)	
900€ - 1,600€	319	1.8 (0.3)		4.9 (0.8)	
1,600€ - 2,200€	329	1.8 (0.4)		4.9 (0.9)	
>2,200€	1,486	1.7 (0.4)		4.9 (0.9)	
Maternal country of birth			<.001		0.7
The Netherlands	1,702	1.7 (0.4)		4.9 (0.9)	
Other Western	252	1.8 (0.4)		4.9 (0.8)	
Non-Western	944	1.8 (0.3)		4.8 (0.7)	
Paternal country of birth			0.006		0.1
The Netherlands	1,419	1.7 (0.4)		4.9 (0.9)	
Other Western	120	1.8 (0.4)		5.0 (1.1)	
Non-Western	502	1.8 (0.4)		4.8 (0.8)	
Family status at intake			0.002		0.006
Married	1,394	1.7 (0.4)		4.8 (0.8)	
Living together	1,023	1.8 (0.4)		4.9 (1.0)	
No partner	292	1.8 (0.3)		4.9 (0.8)	
Maternal parity			<.001		0.001
nulliparous	1,630	1.8 (0.4)		4.9 (0.9)	
1 child	883	1.7 (0.4)		4.8 (0.8)	
2 or more children	338	1.7 (0.4)		4.8 (0.6)	
Maternal smoking use during pregnancy			0.1		0.9
Never	2,004	1.7 (0.4)		4.9 (0.9)	
Smoking use until pregnancy known	222	1.7 (0.4)		4.9 (0.8)	
Continued smoking use during pregnancy	338	1.8 (0.4)		4.9 (0.9)	
Maternal alcohol use during pregnancy			0.3		<.001
Never	973	1.7 (0.4)		4.8 (0.8)	
Alcohol use until pregnancy known	335	1.8 (0.4)		5.0 (1.0)	
Continued alcohol use during pregnancy	1,023	1.7 (0.4)		4.9 (0.9)	
Maternal age at intake (years)	2,954	-0.06	0.001	0.01	0.6
Paternal age at intake (years)	2,077	-0.07	0.001	0.01	0.7
Maternal pre-pregnancy body mass index (kg/m ²)	2,181	0.02	0.2	-0.03	0.1
Paternal body mass index (kg/m ²)	2,070	-0.08	<.001	-0.04	0.043
Maternal height (cm)	2,638	-0.07	<.001	0.04	0.046
Paternal height (cm)	2,074	-0.04	0.1	0.02	0.3
Maternal psychological distress during pregnancy	2,237	0.08	0.029	0.01	0.5
Paternal psychological distress during pregnancy	1,785	0.05	0.029	0.01	0.8
Maternal intelligence quotient score	2,688	-0.06	0.003	0.05	0.007

Abbreviations: OC, organic carbon.

Values are mean (standard deviation) per category using one-way ANOVA test for categorical variables, and are pairwise correlation coefficients for continuous variables

Table S8. Exposure levels to Fe and K during pregnancy by participant characteristics

Participant characteristics	n	Fe	p-value	K	p-value
Maternal education level			<.001		0.009
Primary education or lower	176	121.7 (13.1)		111.5 (4.9)	
Secondary education	1,092	121.6 (18.2)		113.1 (7.8)	
Higher education	1,453	125.2 (21.1)		113.3 (7.2)	
Paternal education level			0.005		0.1
Primary education or lower	92	122.5 (16.2)		111.8 (6.7)	
Secondary education	700	122.5 (22.8)		113.5 (8.3)	
Higher education	1,069	125.8 (21.0)		113.4 (7.1)	
Monthly household income at intake			0.3		<.001
<900€	172	123.0 (17.1)		111.6 (6.3)	
900€ - 1,600€	319	123.1 (16.5)		111.8 (6.4)	
1,600€ - 2,200€	329	123.1 (19.0)		113.8 (7.8)	
>2,200€	1,486	124.8 (21.2)		113.6 (7.7)	
Maternal country of birth			0.9		0.001
The Netherlands	1,702	123.4 (21.0)		113.4 (7.6)	
Other Western	252	124.0 (21.3)		113.3 (7.9)	
Non-Western	944	123.3 (15.0)		112.3 (6.6)	
Paternal country of birth			0.1		0.010
The Netherlands	1,419	124.3 (21.6)		113.6 (7.7)	
Other Western	120	127.4 (28.5)		112.7 (6.5)	
Non-Western	502	123.1 (16.6)		112.5 (7.2)	
Family status at intake			0.024		<.001
Married	1,394	122.5 (17.8)		112.8 (7.3)	
Living together	1,023	124.3 (21.7)		113.7 (7.6)	
No partner	292	125.1 (19.5)		111.8 (5.8)	
Maternal parity			0.046		<.001
nulliparous	1,630	124.4 (21.2)		113.5 (7.5)	
1 child	883	122.7 (17.8)		112.5 (7.0)	
2 or more children	338	122.2 (13.6)		112.1 (6.8)	
Maternal smoking use during pregnancy			0.2		0.8
Never	2,004	123.7 (20.3)		113.1 (7.3)	
Smoking use until pregnancy known	222	124.8 (17.9)		112.9 (7.0)	
Continued smoking use during pregnancy	338	122.1 (16.1)		113.2 (8.2)	
Maternal alcohol use during pregnancy			0.001		0.030
Never	973	122.2 (18.1)		112.8 (7.4)	
Alcohol use until pregnancy known	335	125.3 (22.7)		114.0 (8.1)	
Continued alcohol use during pregnancy	1,023	125.4 (20.2)		113.1 (7.0)	
Maternal age at intake (years)	2,954	0.02	0.2	0.05	0.005
Paternal age at intake (years)	2,077	0.03	0.3	0.00	0.9
Maternal pre-pregnancy body mass index (kg/m ²)	2,181	-0.02	0.3	-0.02	0.4
Paternal body mass index (kg/m ²)	2,070	-0.05	0.039	-0.02	0.4
Maternal height (cm)	2,638	0.03	0.1	0.06	0.002
Paternal height (cm)	2,074	0.00	0.9	0.07	0.002
Maternal psychological distress during pregnancy	2,237	0.01	0.5	-0.02	0.4
Paternal psychological distress during pregnancy	1,785	0.02	0.5	-0.04	0.
Maternal intelligence quotient score	2,688	0.04	0.040	0.05	0.016

Values are mean (standard deviation) per category using one-way ANOVA test for categorical variables, and are pairwise correlation coefficients for continuous variables

Table S9. Exposure levels to Si and Zn during fetal life by participant characteristics

Participant characteristics	n	Si	p-value	Zn	p-value
Maternal education level			0.032		0.007
Primary education or lower	176	92.3 (10.1)		19.3 (2.9)	
Secondary education	1,092	92.2 (13.3)		20.3 (4.4)	
Higher education	1,453	93.8 (17.7)		20.3 (4.1)	
Paternal education level			0.6		0.1
Primary education or lower	92	92.1 (8.8)		19.5 (3.8)	
Secondary education	700	93.6 (19.3)		20.5 (4.7)	
Higher education	1,069	94.0 (17.9)		20.4 (4.1)	
Monthly household income at enrollment			0.7		<.001
<900€	172	93.2 (14.0)		19.3 (3.7)	
900€ - 1,600€	319	92.4 (14.0)		19.4 (3.7)	
1,600€ - 2,200€	329	93.3 (15.9)		20.6 (4.4)	
>2,200€	1,486	93.5 (17.4)		20.6 (4.4)	
Maternal country of birth			0.5		<.001
The Netherlands	1,702	93.1 (16.7)		20.4 (4.3)	
Other Western	252	93.4 (19.2)		20.4 (4.5)	
Non-Western	944	92.4 (10.9)		19.7 (3.8)	
Paternal country of birth			0.2		0.006
The Netherlands	1,419	93.7 (17.9)		20.6 (4.4)	
Other Western	120	95.5 (26.6)		20.0 (3.6)	
Non-Western	502	92.7 (12.6)		19.9 (4.1)	
Family status at enrollment			0.1		<.001
Married	1,394	92.4 (13.3)		20.1 (4.2)	
Living together	1,023	93.6 (18.2)		20.6 (4.3)	
No partner	292	93.8 (16.5)		19.5 (3.4)	
Maternal parity			0.041		<.001
nulliparous	1,630	93.6 (17.6)		20.5 (4.3)	
1 child	883	92.5 (13.8)		19.9 (4.0)	
2 or more children	338	91.5 (9.7)		19.7 (3.9)	
Maternal smoking use during pregnancy			0.3		0.9
Never	2,004	93.2 (16.7)		20.2 (4.2)	
Smoking use until pregnancy known	222	93.4 (13.0)		20.1 (4.0)	
Continued smoking use during pregnancy	338	91.7 (11.0)		20.3 (4.7)	
Maternal alcohol use during pregnancy			0.2		0.026
Never	973	92.6 (14.4)		20.1 (4.2)	
Alcohol use until pregnancy known	335	93.5 (19.4)		20.8 (4.6)	
Continued alcohol use during pregnancy	1,023	93.9 (16.9)		20.2 (4.0)	
Maternal age at enrollment (years)	2,954	-0.03	0.2	0.05	0.003
Paternal age at enrollment (years)	2,077	-0.01	0.8	0.01	0.8
Maternal pre-pregnancy body mass index (kg/m ²)	2,181	-0.02	0.5	-0.02	0.4
Paternal body mass index (kg/m ²)	2,070	-0.03	0.2	-0.01	0.5
Maternal height (cm)	2,638	0.04	0.1	0.06	0.003
Paternal height (cm)	2,074	-0.01	0.8	-0.04	0.1
Maternal psychological distress during pregnancy	2,237	0.01	0.6	-0.02	0.4
Paternal psychological distress during pregnancy	1,785	0.00	0.9	-0.03	0.1
Maternal intelligence quotient score	2,688	0.02	0.3	0.05	0.017

Values are mean (standard deviation) per category using one-way ANOVA test for categorical variables, and are pairwise correlation coefficients for continuous variables

Table S10. Exposure levels to OP_{DTT} and OP_{ESR} during pregnancy by participant characteristics

Participant characteristics	n	OP _{DTT}	p-value	OP _{ESR}	p-value
Maternal education level			<.001		0.031
Primary education or lower	176	1.3 (0.1)		1064.5 (99.5)	
Secondary education	1,092	1.3 (0.1)		1072.3 (203.5)	
Higher education	1,453	1.3 (0.1)		1089.7 (181.2)	
Paternal education level			0.007		0.3
Primary education or lower	92	1.3 (0.1)		1093.3 (248.8)	
Secondary education	700	1.3 (0.1)		1076.3 (212.4)	
Higher education	1,069	1.3 (0.1)		1091.5 (174.7)	
Monthly household income at intake			<.001		1.0
<900€	172	1.3 (0.1)		1085.1 (155.2)	
900€ - 1,600€	319	1.3 (0.1)		1086.9 (170.7)	
1,600€ - 2,200€	329	1.3 (0.1)		1080.5 (165.9)	
>2,200€	1,486	1.3 (0.1)		1086.2 (194.9)	
Maternal country of birth			<.001		0.3
The Netherlands	1,702	1.3 (0.1)		1075.8 (193.9)	
Other Western	252	1.3 (0.1)		1074.2 (157.6)	
Non-Western	944	1.3 (0.1)		1087.3 (169.2)	
Paternal country of birth			0.001		0.2
The Netherlands	1,419	1.3 (0.1)		1082.7 (192.9)	
Other Western	120	1.3 (0.1)		1117.4 (242.5)	
Non-Western	502	1.3 (0.1)		1083.0 (172.3)	
Family status at intake			<.001		0.002
Married	1,394	1.3 (0.1)		1068.7 (168.1)	
Living together	1,023	1.3 (0.1)		1090.8 (206.3)	
No partner	292	1.3 (0.1)		1100.6 (189.4)	
Maternal parity			<.001		0.002
nulliparous	1,630	1.3 (0.1)		1091.2 (198.3)	
1 child	883	1.3 (0.1)		1069.6 (159.0)	
2 or more children	338	1.3 (0.1)		1061.1 (126.8)	
Maternal smoking use during pregnancy			0.038		0.9
Never	2,004	1.3 (0.1)		1080.7 (186.3)	
Smoking use until pregnancy known	222	1.3 (0.1)		1086.2 (160.1)	
Continued smoking use during pregnancy	338	1.3 (0.1)		1083.2 (211.7)	
Maternal alcohol use during pregnancy			<.001		0.014
Never	973	1.3 (0.1)		1071.6 (174.8)	
Alcohol use until pregnancy known	335	1.3 (0.1)		1098.3 (215.9)	
Continued alcohol use during pregnancy	1,023	1.3 (0.1)		1092.6 (182.9)	
Maternal age at intake (years)	2,954	-0.14	<.001	-0.00	0.9
Paternal age at intake (years)	2,077	-0.11	<.001	-0.00	0.9
Maternal pre-pregnancy body mass index (kg/m ²)	2,181	0.05	0.029	-0.03	0.1
Paternal body mass index (kg/m ²)	2,070	-0.05	0.031	-0.06	0.006
Maternal height (cm)	2,638	-0.09	<.001	0.02	0.3
Paternal height (cm)	2,074	-0.07	0.001	-0.01	0.5
Maternal psychological distress during pregnancy	2,237	0.12	<.001	0.04	0.036
Paternal psychological distress during pregnancy	1,785	0.06	0.015	0.03	0.2
Maternal intelligence quotient score	2,688	-0.11	<.001	0.02	0.4

Abbreviations: OP, oxidative potential (evaluated using two acellular methods: OP_{DTT} – dithiothreitol and OP_{ESR} – electron spin resonance).

Values are mean (standard deviation) per category using one-way ANOVA test for categorical variables, and are pairwise correlation coefficients for continuous variables

Table S11. Exposure levels to UFP during pregnancy by participant characteristics

Participant characteristics	n	UFP	p-value
Maternal education level			<.001
Primary education or lower	176	10141.3 (1153.8)	
Secondary education	1,092	10148.3 (1743.0)	
Higher education	1,453	10513.9 (1933.5)	
Paternal education level			<.001
Primary education or lower	92	10152.7 (1398.8)	
Secondary education	700	10223.9 (2067.4)	
Higher education	1,069	10583.7 (1928.8)	
Monthly household income at intake			0.5
<900€	172	10247.4 (1524.5)	
900€ - 1,600€	319	10358.0 (1507.4)	
1,600€ - 2,200€	329	10381.3 (1821.2)	
>2,200€	1,486	10450.1 (1965.9)	
Maternal country of birth			0.8
The Netherlands	1,702	10326.9 (1979.4)	
Other Western	252	10393.3 (1819.6)	
Non-Western	944	10316.4 (1417.5)	
Paternal country of birth			0.1
The Netherlands	1,419	10430.6 (2013.3)	
Other Western	120	10659.4 (2357.3)	
Non-Western	502	10297.4 (1534.2)	
Family status at intake			0.003
Married	1,394	10221.4 (1695.7)	
Living together	1,023	10458.8 (2013.0)	
No partner	292	10449.9 (1598.9)	
Maternal parity			0.002
nulliparous	1,630	10459.5 (1954.4)	
1 child	883	10215.7 (1666.5)	
2 or more children	338	10227.8 (1296.9)	
Maternal smoking use during pregnancy			0.6
Never	2,004	10353.4 (1864.3)	
Smoking use until pregnancy known	222	10427.3 (1750.2)	
Continued smoking use during pregnancy	338	10271.2 (1616.8)	
Maternal alcohol use during pregnancy			<.001
Never	973	10203.5 (1700.2)	
Alcohol use until pregnancy known	335	10547.1 (2016.4)	
Continued alcohol use during pregnancy	1,023	10518.5 (1874.5)	
Maternal age at intake (years)	2,954	0.02	0.4
Paternal age at intake (years)	2,077	0.01	0.5
Maternal pre-pregnancy body mass index (kg/m ²)	2,181	-0.02	0.3
Paternal body mass index (kg/m ²)	2,070	-0.04	0.1
Maternal height (cm)	2,638	0.02	0.3
Paternal height (cm)	2,074	0.02	0.4
Maternal psychological distress during pregnancy	2,237	0.01	0.8
Paternal psychological distress during pregnancy	1,785	0.00	0.9
Maternal intelligence quotient score	2,688	0.06	0.002

Abbreviations: UFP, ultra fine particles.

Values are mean (standard deviation) per category using one-way ANOVA test for categorical variables, and are pairwise correlation coefficients for continuous variables

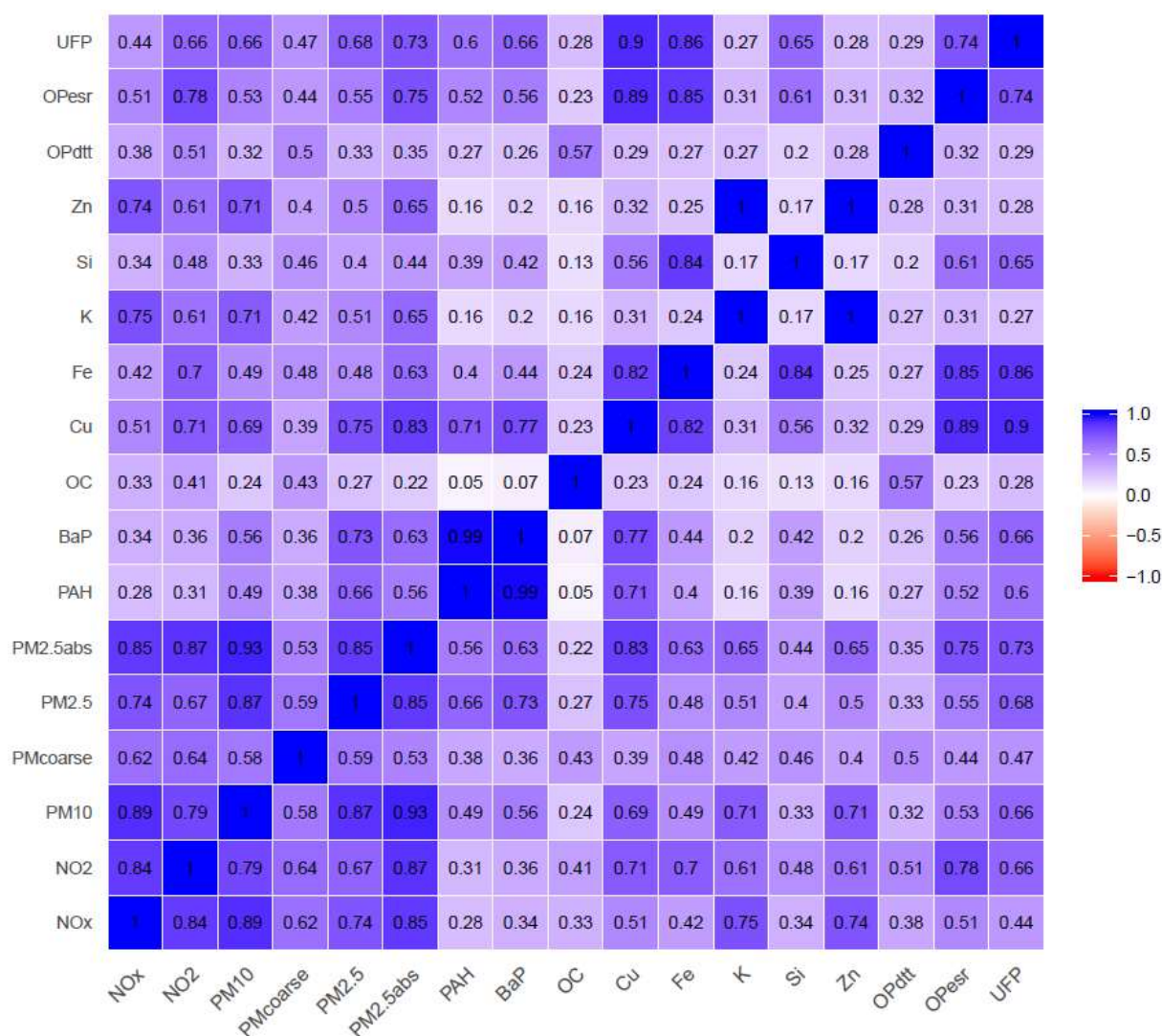


Figure S2. Correlations between levels of the pollutants during pregnancy

Abbreviations: NO_x, nitrogen oxides; NO₂, nitrogen dioxide; PM, particulate matter with different aerodynamic diameters: less than 10µm (PM₁₀); between 10µm and 2.5µm (PMcoarse); less than 2.5µm (PM_{2.5}); PM_{2.5}abs, absorbance of PM_{2.5} filters; PAHs, polycyclic aromatic hydrocarbons; B[a]P, benzo[a]pyrene; OC, organic carbon; OP, oxidative potential (evaluated using two acellular methods: OP_{DTT} – dithiothreitol and OP_{ESR} – electron spin resonance); UFP, ultra-fine particles.

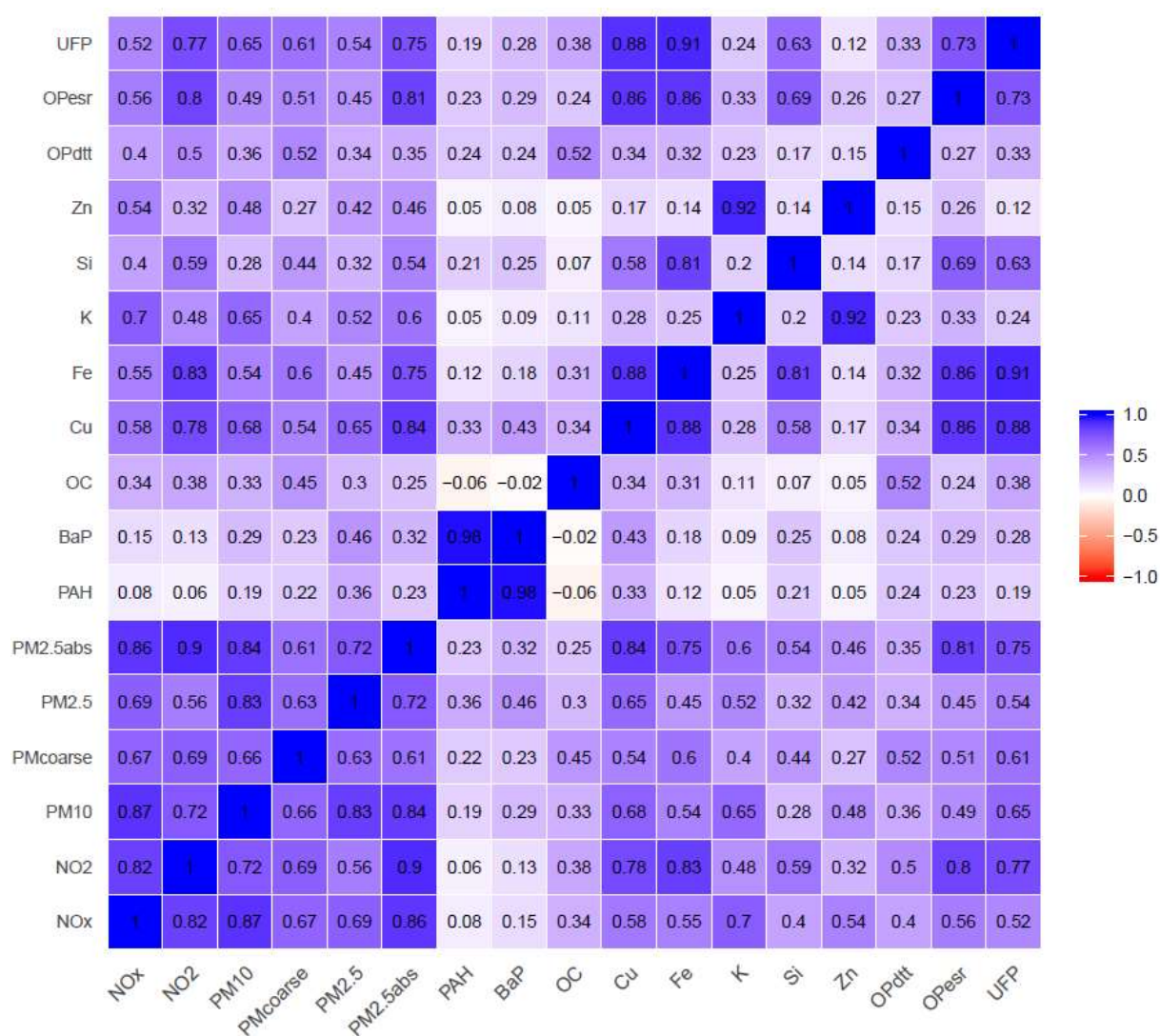


Figure S3. Correlations between levels of the pollutants during childhood

Abbreviations: NO_x, nitrogen oxides; NO₂, nitrogen dioxide; PM, particulate matter with different aerodynamic diameters: less than 10µm (PM₁₀); between 10µm and 2.5µm (PMcoarse); less than 2.5µm (PM_{2.5}); PM_{2.5}abs, absorbance of PM_{2.5} filters; PAHs, polycyclic aromatic hydrocarbons; B[a]P, benzo[a]pyrene; OC, organic carbon; OP, oxidative potential (evaluated using two acellular methods: OP_{DTT} – dithiothreitol and OP_{ESR} – electron spin resonance); UFP, ultra-fine particles.

Table S12. Results of multi-pollutant models selected by the Deletion/Substitution/Addition algorithm for pregnancy exposures in relation to global fractional anisotropy and global mean diffusivity, respectively, excluding participants of mothers recruited after birth (n=310)

		Contrast	Coef. (95% CI)	p-value
Global fractional anisotropy				
Pregnancy exposure models (% of runs)				
Model 1 (24.5%)				
	PM _{2.5}	5 µg/m ³	-1.53 (-2.34 ; -0.73)	<0.001
	PAHs	1 ng/m ³	0.33 (0.05 ; 0.61)	0.022
	OP _{DTT}	1 nmol DTT/min/m ³	0.52 (-0.08 ; 1.12)	0.1
Model 2 (20%)				
	PM _{2.5}	5 µg/m ³	-1.36 (-2.14 ; -0.58)	0.001
	PAHs	1 ng/m ³	0.33 (0.05 ; 0.62)	0.020
Model 3 (13%)				
	PM _{2.5}	5 µg/m ³	-0.73 (-1.29 ; -0.16)	0.012
Global mean diffusivity				
Pregnancy exposure models (% of runs)				
Model 1 (13.5%)				
	Si	100 ng/m ³	0.05 (0.00 ; 0.11)	0.049
	OP _{DTT}	1 nmol DTT/min/m ³	0.06 (-0.02 ; 0.13)	0.1

Abbreviations: Coef, coefficient; CI, confidence intervals; DSA, Deletion/Substitution/Addition; OP_{DTT}, oxidative potential of PM_{2.5} (DTT: evaluated using dithiothreitol); PAHs, polycyclic aromatic hydrocarbons; PM_{2.5}, particulate matter with diameter of less than 2.5µm. Model selection is performed using Deletion/Substitution/Addition algorithm. PM₁₀, B[a]P, K, and UFP were excluded due to a correlation of 0.90 or more with PM_{2.5} absorbance, PAHs, Zn, and Cu respectively. For each combination of period of exposure and outcome, 200 runs were performed and the final model was selected based on frequency of occurrence (% of runs, at least 10% to be reported here). Coefficients and 95% CI from (multiple) linear regression models adjusted for both maternal and paternal education, country of birth, age, height, BMI, and psychological distress during pregnancy; maternal smoking and alcohol consumption during pregnancy, parity, marital status, intelligence quotient, and household income; and child's genetic ancestry, gender, and age at the scanning session. Any missing covariates were imputed through multiple imputation, and inverse probability weighting technique was used to account for potential selection bias.

Table S13. Results of analyses in which pregnancy and childhood exposures that were selected by Deletion/Substitution/Addition algorithm, and were nominally significant in the single pollutant models, were introduced simultaneously in the model in relation to global fractional anisotropy and global mean diffusivity, respectively.

	Contrast	Coef. (95% CI)	p-value
Global fractional anisotropy			
pregnancy PM _{2.5}	5 µg/m ³	-0.48 (-1.07 ; 0.10)	0.1
childhood NO _x	20 µg/m ³	-0.10 (-0.21 ; 0.00)	0.1
Global mean diffusivity			
pregnancy Si	100 ng/m ³	0.06 (0.01 ; 0.11)	0.024
childhood Zn	10 ng/m ³	0.02 (0.01 ; 0.04)	0.009
childhood OP _{DTT}	1 nmol DTT/min/m ³	0.06 (-0.01 ; 0.13)	0.1

Abbreviations: Coef., coefficient; CI, confidence intervals; PM_{2.5}, particulate matter with diameter of <2.5µm; NO_x, nitrogen oxides; OP_{DTT}, oxidative potential of PM_{2.5} (DTT: evaluated using dithiothreitol). Coefficients and 95% CI from multiple linear regression models adjusted for both maternal and paternal education, country of birth, age, height, BMI, and psychological distress during pregnancy; maternal smoking and alcohol consumption during pregnancy, parity, marital status, intelligence quotient, and household income; and child's genetic ancestry, gender, and age at the scanning session. Any missing covariates were imputed through multiple imputation, and inverse probability weighting technique was used to account for potential selection bias.

Table S14. Adjusted linear regression analyses of fractional anisotropy in twelve individual white matter tracts in relation to pregnancy PM_{2.5}, and childhood NO_x exposures

Fractional anisotropy	Pregnancy exposure to PM _{2.5}				
	Coef.	95% CI		p-value	q-value
uncinate fasciculus left hemisphere	-0.00892	-0.01808	; 0.00023	0.1	0.1
uncinate fasciculus right hemisphere	-0.00467	-0.01283	; 0.00349	0.3	0.4
cingulate gyrus part of cingulum left hemisphere	-0.00987	-0.02302	; 0.00328	0.1	0.2
cingulate gyrus part of cingulum right hemisphere	-0.00622	-0.01810	; 0.00566	0.3	0.4
superior longitudinal fasciculus left hemisphere	-0.00585	-0.01260	; 0.00090	0.1	0.2
superior longitudinal fasciculus right hemisphere	-0.00878	-0.01601	; -0.00154	0.018	0.1
forceps minor	-0.01276	-0.02261	; -0.00291	0.012	0.1
forceps major	-0.00297	-0.01350	; 0.00757	0.6	0.6
inferior longitudinal fasciculus left hemisphere	-0.00286	-0.00946	; 0.00373	0.4	0.5
inferior longitudinal fasciculus right hemisphere	-0.00199	-0.00880	; 0.00483	0.6	0.6
corticospinal tract left hemisphere	-0.00754	-0.01389	; -0.00119	0.020	0.1
corticospinal tract right hemisphere	-0.00800	-0.01440	; -0.00161	0.015	0.1

Fractional anisotropy	Childhood exposure to NO _x				
	Coef.	95% CI		p-value	q-value
uncinate fasciculus left hemisphere	-0.00184	-0.00346	; -0.00022	0.027	0.1
uncinate fasciculus right hemisphere	-0.00165	-0.00309	; -0.00021	0.026	0.1
cingulate gyrus part of cingulum left hemisphere	-0.00175	-0.00408	; 0.00057	0.1	0.2
cingulate gyrus part of cingulum right hemisphere	0.00015	-0.00195	; 0.00226	0.9	0.9
superior longitudinal fasciculus left hemisphere	-0.00062	-0.00182	; 0.00057	0.3	0.4
superior longitudinal fasciculus right hemisphere	-0.00165	-0.00293	; -0.00037	0.012	0.1
forceps minor	-0.00173	-0.00348	; 0.00001	0.1	0.1
forceps major	-0.00025	-0.00211	; 0.00162	0.8	0.9
inferior longitudinal fasciculus left hemisphere	-0.00102	-0.00219	; 0.00015	0.1	0.1
inferior longitudinal fasciculus right hemisphere	-0.00145	-0.00266	; -0.00024	0.019	0.1
corticospinal tract left hemisphere	-0.00129	-0.00241	; -0.00017	0.024	0.1
corticospinal tract right hemisphere	-0.00070	-0.00183	; 0.00043	0.2	0.3

Abbreviations: Coef, coefficient; CI, confidence intervals; NO_x, nitrogen oxides; PM_{2.5}, particulate matter with diameter of <2.5µm. Coefficients and 95% CI from linear regression models adjusted for both maternal and paternal education, country of birth, age, height, BMI, and psychological distress during pregnancy; maternal smoking and alcohol consumption during pregnancy, parity, marital status, intelligence quotient, and household income; and child's genetic ancestry, gender, and age at the scanning session. Any missing covariates were imputed through multiple imputation, and inverse probability weighting technique was used to account for potential selection bias.

Pregnancy PM_{2.5} (5µg/m³ increment) and childhood NO_x (20µg/m³ increment) were selected for this analysis as significant predictors of global FA (nominal p<0.05) in DSA-selected multipollutant models of pregnancy or childhood exposures (respectively), and as significant predictors of global FA in the single pollutant models.

To obtain the q-value, false discovery rate correction for multiple testing was applied using Benjamini and Hochberg method (Benjamini and Hochberg 1995).

The FDR significant exposures were then included in multipollutant models of individual white matter tracts

Table S15. Adjusted linear regression analyses of mean diffusivity in twelve individual white matter tracts in relation to pregnancy Si, and childhood Zn and OP_{DTT} exposures

Mean diffusivity**	Pregnancy exposure to Si				
	Coef.	95% CI		p-value	q-value
uncinate fasciculus left hemisphere	0.00259	-0.00258	; 0.00775	0.3	0.4
uncinate fasciculus right hemisphere	0.00359	-0.00153	; 0.00872	0.2	0.3
cingulate gyrus part of cingulum left hemisphere	0.00934	0.00249	; 0.01619	0.008	0.032
cingulate gyrus part of cingulum right hemisphere	0.00761	0.00089	; 0.01434	0.027	0.1
superior longitudinal fasciculus left hemisphere	0.00892	0.00350	; 0.01434	0.002	0.012
superior longitudinal fasciculus right hemisphere	0.00610	-0.00008	; 0.01229	0.1	0.1
forceps minor	0.01690	0.00945	; 0.02435	<.001	<.001
forceps major	-0.00089	-0.01650	; 0.01472	0.9	0.9
inferior longitudinal fasciculus left hemisphere	0.00699	0.00034	; 0.01364	0.040	0.1
inferior longitudinal fasciculus right hemisphere	0.00680	-0.00072	; 0.01432	0.1	0.1
corticospinal tract left hemisphere	0.00207	-0.00861	; 0.01275	0.7	0.8
corticospinal tract right hemisphere	-0.00102	-0.01111	; 0.00907	0.8	0.9
Mean diffusivity**	Childhood exposure to Zn				
	Coef.	95% CI		p-value	q-value
uncinate fasciculus left hemisphere	0.00184	0.00004	; 0.00365	0.5	0.1
uncinate fasciculus right hemisphere	0.00242	0.00063	; 0.00421	0.009	0.018
cingulate gyrus part of cingulum left hemisphere	0.00439	0.00199	; 0.00679	<.001	<.001
cingulate gyrus part of cingulum right hemisphere	0.00359	0.00123	; 0.00594	0.003	0.012
superior longitudinal fasciculus left hemisphere	0.00256	0.00066	; 0.00445	0.009	0.018
superior longitudinal fasciculus right hemisphere	0.00305	0.00089	; 0.00522	0.006	0.018
forceps minor	0.00460	0.00199	; 0.00721	0.001	0.006
forceps major	0.00030	-0.00518	; 0.00577	0.9	0.9
inferior longitudinal fasciculus left hemisphere	0.00248	0.00015	; 0.00481	0.037	0.1
inferior longitudinal fasciculus right hemisphere	0.00286	0.00022	; 0.00549	0.034	0.1
corticospinal tract left hemisphere	0.00101	-0.00272	; 0.00475	0.6	0.6
corticospinal tract right hemisphere	0.00247	-0.00105	; 0.00600	0.2	0.2
Mean diffusivity**	Childhood exposure to OP _{DTT}				
	Coef.	95% CI		p-value	q-value
uncinate fasciculus left hemisphere	0.00383	-0.00295	; 0.01060	0.3	0.5
uncinate fasciculus right hemisphere	0.00245	-0.00428	; 0.00917	0.5	0.5
cingulate gyrus part of cingulum left hemisphere	0.01008	0.00111	; 0.01905	0.028	0.3
cingulate gyrus part of cingulum right hemisphere	0.00737	-0.00144	; 0.01617	0.1	0.3
superior longitudinal fasciculus left hemisphere	0.00292	-0.00417	; 0.01001	0.4	0.5
superior longitudinal fasciculus right hemisphere	0.00526	-0.00283	; 0.01335	0.2	0.5
forceps minor	0.00799	-0.00176	; 0.01773	0.1	0.3
forceps major	0.00803	-0.01236	; 0.02843	0.4	0.5
inferior longitudinal fasciculus left hemisphere	0.00745	-0.00127	; 0.01616	0.1	0.3
inferior longitudinal fasciculus right hemisphere	0.00558	-0.00428	; 0.01544	0.3	0.5
corticospinal tract left hemisphere	0.00597	-0.00796	; 0.01989	0.4	0.5
corticospinal tract right hemisphere	0.00209	-0.01115	; 0.01532	0.8	0.8

Abbreviations: Coef, coefficient; CI, confidence intervals; OP_{DTT}, oxidative potential of PM_{2.5} (DTT: evaluated using dithiothreitol). Coefficients and 95% CI from linear regression models adjusted for both maternal and paternal education, country of birth, age, height, BMI, and psychological distress during pregnancy; maternal smoking and alcohol consumption during pregnancy, parity, marital status, intelligence quotient, and household income; and child's genetic ancestry, gender, and age at the scanning session. Any missing covariates were imputed through multiple imputation, and inverse probability weighting technique was used to account for potential selection bias.

Pregnancy Si (100 ng/m³ increment) and childhood Zn (10 ng/m³ increment) and OP_{DTT} (1 nmol DTT/min/m³ increment) were selected for this analysis as significant predictors of global MD (nominal p<0.05) in DSA-selected multipollutant models of pregnancy or childhood exposures (respectively), and as significant predictors of global MD in the single pollutant models.

To obtain the q-value, false discovery rate correction for multiple testing was applied using Benjamini and Hochberg method (Benjamini and Hochberg 1995).

The FDR significant exposures were then included in multipollutant models of individual white matter tracts

*Values of MD were multiplied by 10⁹ (concerns only individual tracts analyses)

Table S16. Results of analyses in which pregnancy and childhood exposures selected by Deletion/Substitution/Addition algorithm were introduced simultaneously in the model in relation to global mean diffusivity in three white matter tracts

	Contrast	Coef. (95% CI)	p-value
Mean diffusivity in:			
Cingulate gyrus part of cingulum of the left hemisphere			
pregnancy Si	100 ng/m ³	0.0082 (0.0015 ; 0.0151)	0.017
childhood Zn	10 ng/m ³	0.0041 (0.0017 ; 0.0065)	0.001
Superior longitudinal fasciculus of the left hemisphere			
pregnancy Si	100 ng/m ³	0.0083 (0.0030 ; 0.0137)	0.002
childhood Zn	10 ng/m ³	0.0023 (0.0004 ; 0.0042)	0.016
Forceps minor			
pregnancy Si	100 ng/m ³	0.0158 (0.0085 ; 0.0232)	<.001
childhood Zn	10 ng/m ³	0.0041 (0.0015 ; 0.0067)	0.002

Abbreviations: Coef., coefficient; CI, confidence intervals; PM_{2.5}, particulate matter with diameter of <2.5µm; NO_x, nitrogen oxides; OP_{DTT}, oxidative potential of PM_{2.5} (DTT: evaluated using dithiothreitol). Coefficients and 95% CI from multiple linear regression models adjusted for both maternal and paternal education, country of birth, age, height, BMI, and psychological distress during pregnancy; maternal smoking and alcohol consumption during pregnancy, parity, marital status, intelligence quotient, and household income; and child's genetic ancestry, gender, and age at the scanning session. Any missing covariates were imputed through multiple imputation, and inverse probability weighting technique was used to account for potential selection bias.

The selection of the pollutants is based on FDR-significance in single-pollutant models. If more than one pollutant was FDR-significant for FA or MD in the same tract, multi-pollutant models were performed for FA or MD in the tract.

Table S17. Results of the adjusted associations between exposure during pregnancy and childhood to single air pollutants and global fractional anisotropy, and global mean diffusivity at 9-12y, with and without accounting for measurement error

Fractional anisotropy																
pollutant	Pregnancy					Childhood										
	original results			with measurement error		original results			with measurement error							
	95% CI		stderr	95% CI		stderr	95% CI		stderr	95% CI		stderr				
NO _x	-0.20	;	-0.02	0.045	-0.19	;	-0.01	0.046	-0.23	;	-0.04	0.049	-0.23	;	-0.04	0.050
NO ₂	-0.25	;	0.03	0.068	-0.24	;	0.02	0.068	-0.25	;	-0.01	0.059	-0.25	;	-0.02	0.060
PM ₁₀	-0.90	;	-0.08	0.205	-0.99	;	-0.03	0.245	-0.91	;	0.01	0.232	-1.12	;	-0.04	0.275
PM _{coarse}	-0.37	;	0.27	0.161	-0.38	;	0.26	0.164	-0.63	;	0.04	0.169	-0.65	;	0.00	0.167
PM ₂₅	-1.26	;	-0.16	0.277	-0.99	;	-0.11	0.224	-1.14	;	0.21	0.340	-1.06	;	0.14	0.306
PM ₂₅ abs	-0.51	;	-0.07	0.113	-0.51	;	-0.05	0.119	-0.51	;	-0.02	0.122	-0.51	;	-0.03	0.122
Cu	-0.71	;	0.06	0.193	-0.69	;	0.05	0.189	-0.65	;	0.21	0.217	-0.66	;	0.18	0.215
Fe	-0.54	;	0.14	0.172	-0.55	;	0.14	0.175	-0.53	;	0.09	0.156	-0.55	;	0.06	0.155
K	-0.84	;	0.08	0.230	-0.97	;	0.25	0.310	-1.03	;	-0.03	0.253	-0.70	;	0.17	0.221
Si	-0.70	;	0.15	0.214	-0.73	;	0.15	0.225	-0.66	;	0.19	0.216	-0.34	;	0.06	0.102
Zn	-0.28	;	0.04	0.081	-0.48	;	0.20	0.174	-0.27	;	0.02	0.075	-0.18	;	0.00	0.047
Mean diffusivity																
pollutant	Pregnancy					Childhood										
	original results			with measurement error		original results			with measurement error							
	95% CI		stderr	95% CI		stderr	95% CI		stderr	95% CI		stderr				
NO _x	0.00	;	0.02	0.005	0.00	;	0.02	0.006	0.01	;	0.03	0.006	0.01	;	0.03	0.007
NO ₂	0.00	;	0.04	0.008	0.00	;	0.04	0.009	0.00	;	0.03	0.007	0.01	;	0.03	0.006
PM ₁₀	0.00	;	0.10	0.025	0.00	;	0.11	0.030	0.01	;	0.12	0.028	0.01	;	0.14	0.032
PM _{coarse}	-0.01	;	0.07	0.020	-0.02	;	0.06	0.019	0.00	;	0.09	0.021	0.00	;	0.08	0.021
PM ₂₅	0.02	;	0.15	0.034	0.01	;	0.12	0.028	0.03	;	0.20	0.041	0.02	;	0.18	0.040
PM ₂₅ abs	0.01	;	0.06	0.014	0.01	;	0.06	0.015	0.01	;	0.07	0.015	0.01	;	0.07	0.015
Cu	0.01	;	0.10	0.023	0.01	;	0.10	0.024	-0.02	;	0.09	0.026	-0.02	;	0.09	0.027
Fe	0.01	;	0.09	0.021	0.01	;	0.09	0.021	-0.01	;	0.07	0.019	0.00	;	0.07	0.018
K	-0.02	;	0.09	0.028	-0.04	;	0.12	0.042	0.03	;	0.15	0.031	0.01	;	0.17	0.042
Si	0.02	;	0.12	0.026	0.01	;	0.13	0.031	0.00	;	0.11	0.026	0.00	;	0.11	0.027
Zn	-0.01	;	0.03	0.010	-0.02	;	0.06	0.022	0.01	;	0.05	0.009	0.01	;	0.06	0.013

Coef, coefficient; CI, confidence intervals; stderr, standard error; NO_x, nitrogen oxides; NO₂, nitrogen dioxide; PM, particulate matter with different aerodynamic diameters: less than 10µm (PM₁₀); between 10µm and 2.5µm (PM_{coarse}); less than 2.5µm (PM_{2.5}); PM_{2.5}absorbance, absorbance of PM_{2.5} filters. Coefficients and 95% CI from linear regression models adjusted for both maternal and paternal education, country of birth, age, height, BMI, and psychological distress during pregnancy; maternal smoking and alcohol consumption during pregnancy, parity, marital status, intelligence quotient, and household income; and child's genetic ancestry, gender, and age at the scanning session. Any missing covariates were imputed through multiple imputation, and inverse probability weighting technique was used to account for potential selection bias.