

SUPPLEMENTARY MATERIAL

Prenatal and childhood exposure to ambient air pollution and cognitive function in school-age children: examining sensitive windows and sex-specific associations

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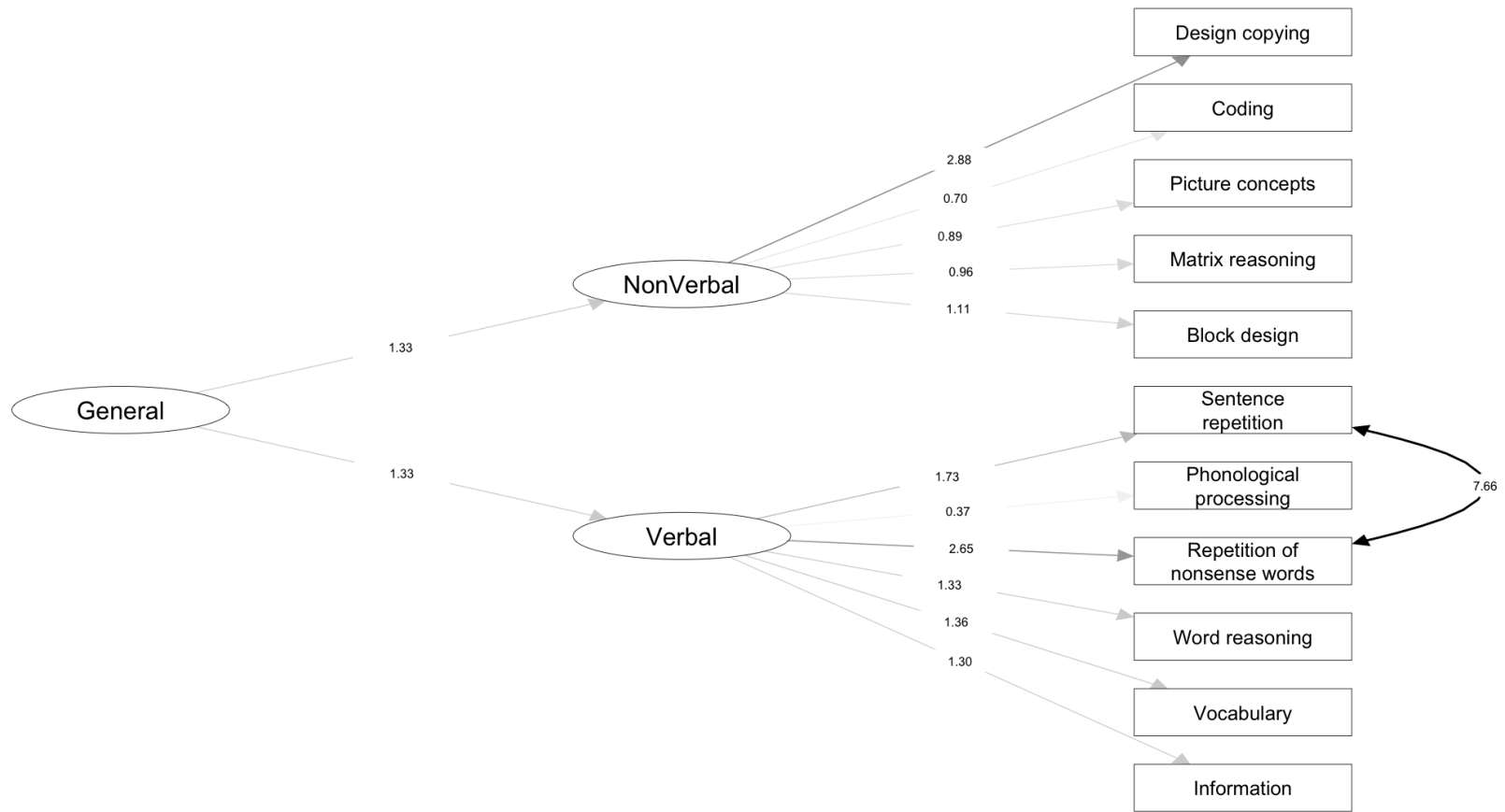


Figure S1: Latent path model of cognitive abilities for the EDEN cohort

Constructed using Confirmatory Factor Analyses and considering a two-factor second order structure.

Ellipses denote the latent constructs while rectangles denote the observed variables. The numbers correspond to the estimate of the latent path model.

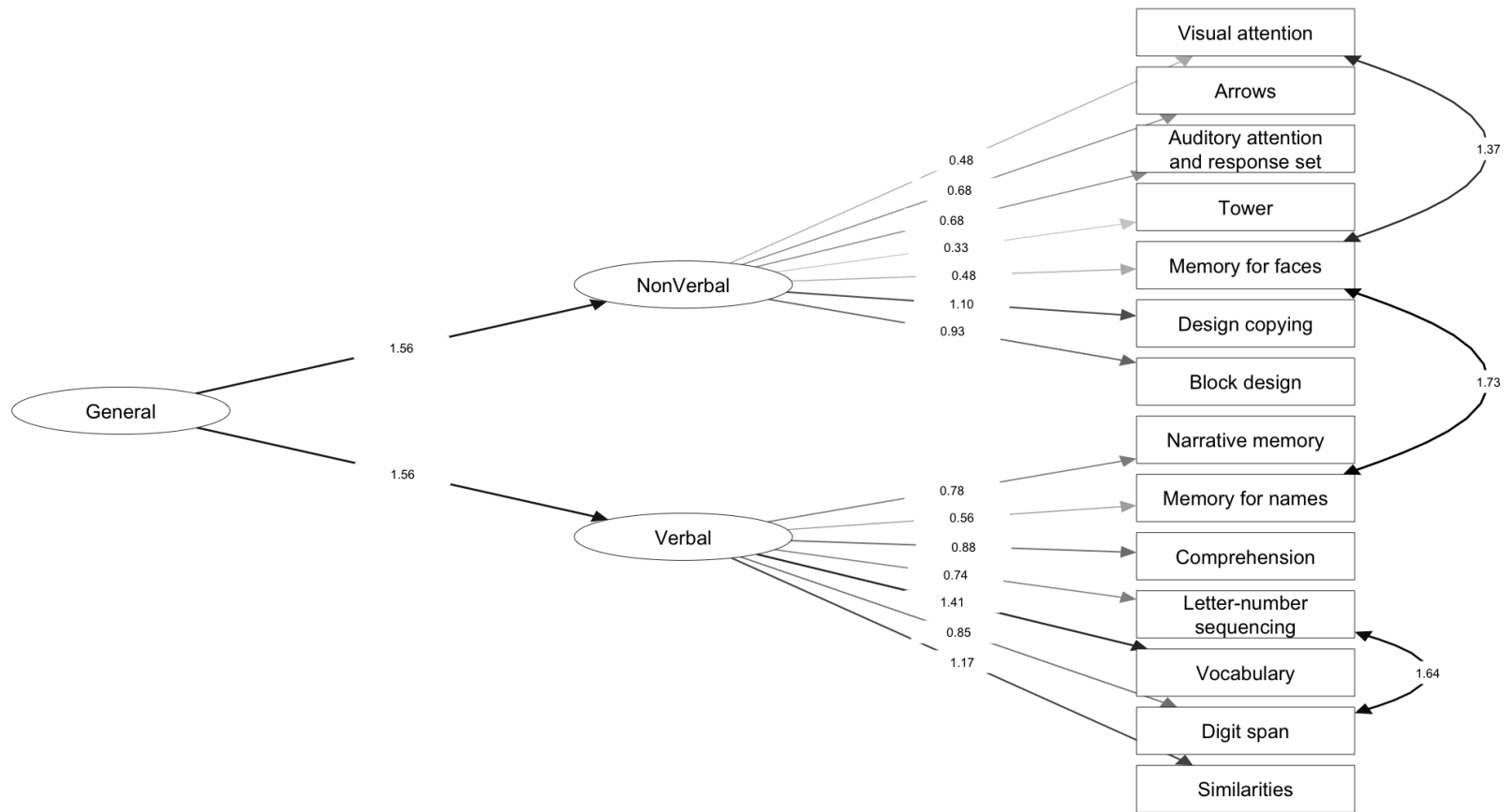


Figure S2: Latent path model of cognitive abilities for the PELAGIE cohort

Constructed using Confirmatory Factor Analyses and considering a two-factor second order structure.

Ellipses denote the latent constructs while rectangles denote the observed variables. The numbers correspond to the estimate of the latent path model.

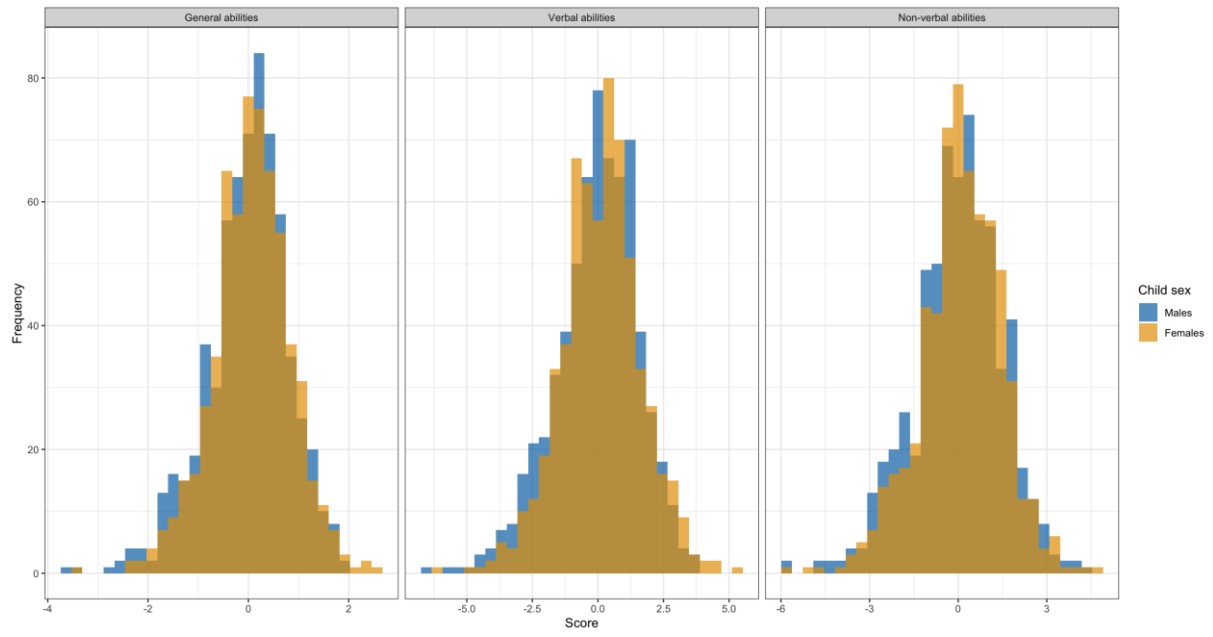


Figure S3: Distribution of cognitive scores at 5-6 years
n = 1271 mother-child pairs from the EDEN and PELAGIE cohorts.
The overlapping distribution for males and females appears as an intermediate color.

Table S1: Comparison of the included and not included participants in the main analyses

Characteristics	Included	Not included	Pvalue ^b
	(n = 1271)	(n = 4053)	
	n (%)		
Cohort			<0.001
EDEN	1003 (79)	999 (25)	
PELAGIE	268 (21)	3054 (75)	
Sex			0.97
Male	650 (51)	2018 (51)	
Female	621 (49)	1936 (49)	
Highest level of parental education			0.07
Baccalaureate or less	495 (39)	1628 (41)	
Baccalaureate +1 or + 2 years	312 (25)	1042 (26)	
Baccalaureate + 3 years (bachelor) or more	449 (36)	1271 (32)	
Mother's BMI before pregnancy (kg/m ²)			<0.001
Underweight (< 18.5)	99 (8)	307 (8)	
Normal weight (≥ 18.5 and < 25)	829 (66)	2874 (73)	
Overweight (≥ 25 and < 30)	227 (18)	518 (13)	
Obese (≥ 30)	96 (8)	231 (6)	
Parity			0.85
No child	562 (44)	1759 (45)	
One child or more	708 (56)	2185 (55)	
Mother's fish consumption before pregnancy			0.08
Less than twice/week	975 (77)	2982 (74)	
Twice/week or more	292 (23)	1021 (26)	
Mother's tobacco consumption during pregnancy			0.07
No	915 (78)	1622 (76)	
Yes	252 (22)	526 (24)	
Breastfeeding			0.04
Breastfed less than 6 months	948 (75)	1992 (78)	
Breastfed 6 months or more	323 (25)	573 (22)	
Mode of day care at 24 months			<0.001
Collective childcare facility	242 (24)	314 (15)	
Childminder or neighbor	587 (57)	1256 (60)	
Family	193 (19)	508 (24)	
	Median (IQR)		
Mother's age at conception (Years)	29.6 (26.7, 32.6)	29.3 (26.3, 32.4)	0.07
Maternal stimulation at 24 months	4.3 (4.0, 5.0)	4.3 (4.0, 5.0)	0.42
HOME score at 5-6 years	0.2 (-0.5, 0.8)	0.3 (-0.5, 0.8)	0.92
Deprivation index	-1.8 (-3.3, 0.0)	-2.0 (-3.3, -0.7)	0.01
PM ₁₀ concentration (µg/m ³) ^a	19.3 (18.3, 20.0)	16.9 (16.2, 17.9)	<0.001
PM _{2.5} concentration (µg/m ³) ^a	12.4 (11.6, 13.1)	11.2 (10.7, 11.9)	<0.001
NO ₂ concentration (µg/m ³) ^a	16.9 (15.5, 19.7)	15.4 (14.2, 17.3)	<0.001

Abbreviations: BMI: body mass index; IQR: InterQuartile Range

^a Average from the conception until the 60th month of life; ^b Chi test for categorical variables and Wilcoxon test for continuous variables (because some variables not normally distributed; comparison restricted to participants with neurodevelopmental data for air pollution and deprivation exposure)

Comparison before imputation

Table S2: Comparison of the imputed and not imputed datasets

Characteristics	Not imputed dataset	Imputed dataset	Pvalue ^a
	n = 1271	n = 1271	
	n (%)		
Cohort			1
EDEN	1003 (79)	1003 (79)	
PELAGIE	268 (21)	268 (21)	
Sex			1
Male	650 (51)	650 (51)	
Female	621 (49)	621 (49)	
Highest level of parental education			1
Baccalaureate or less	495 (39)	502 (39)	
Baccalaureate +1 or + 2 years	312 (25)	316 (25)	
Baccalaureate + 3 years (bachelor) or more	449 (36)	453 (36)	
Missing	15 (1)	0 (0)	
Mother's BMI before pregnancy (kg/m ²)			1
Underweight (< 18.5)	99 (8)	100 (8)	
Normal weight (≥ 18.5 and < 25)	829 (66)	843 (66)	
Overweight (≥ 25 and < 30)	227 (18)	230 (18)	
Obese (≥ 30)	96 (8)	98 (8)	
Missing	20 (2)	0 (0)	
Parity			1
No child	562 (44)	563 (44)	
One child or more	708 (56)	708 (56)	
Missing	1 (1)	0 (0)	
Mother's fish consumption before pregnancy			1
Less than twice/week	975 (77)	978 (77)	
Twice/week or more	292 (23)	293 (23)	
Missing	4 (0.31%)	0 (0.00%)	
Mother's tobacco consumption during pregnancy			0.91
No	915 (78)	1000 (79)	
Yes	252 (22)	271 (21)	
Missing	104 (8)	0 (0)	
Breastfeeding			1
Breastfed less than 6 months	948 (75)	948 (75)	
Breastfed 6 months or more	323 (25)	323 (25)	
Mode of day care at 24 months			0.75
Collective childcare facility	242 (24)	284 (22)	
Childminder or neighbor	587 (57)	741 (58)	
Family	193 (19)	246 (19)	
Missing	249 (20)	0 (0)	
	Median (IQR)		
Mother's age at conception (Years)	29.6 (26.7, 32.6)	29.6 (26.7, 32.6)	1
Maternal stimulation at 24 months	4.3 (4.0, 5.0)	4.3 (4.0, 5.0)	0.90
Missing (n, %)	188 (15)	0 (0)	
HOME score at 5-6 years	0.2 (-0.5, 0.8)	0.2 (-0.5, 0.8)	0.80
Missing (n, %)	31 (2)	0 (0.00%)	
Deprivation index	-1.8 (-3.3, 0.0)	-1.8 (-3.3, 0.0)	1

Abbreviations: BMI: body mass index; IQR: InterQuartile Range

^a Chi test for categorical variables and Wilcoxon test for continuous variables (because some variables not normally distributed)

Table S3: Comparison of the included and not included participants in the sensitivity analyses

Characteristics	Included (n = 1192)	Not included (n = 79)	Pvalue ^b
	n (%)		
Cohort			<0.001
EDEN	950 (80)	53 (67)	
PELAGIE	242 (20)	26 (33)	
Sex			0.98
Male	609 (51)	41 (52)	
Female	583 (49)	38 (48)	
Highest level of parental education			<0.11
Baccalaureate or less	462 (39)	40 (51)	
Baccalaureate +1 or + 2 years	301 (25)	15 (19)	
Baccalaureate + 3 years (bachelor) or more	429 (36)	24 (30)	
Mother's BMI before pregnancy (kg/m ²)			0.46
Underweight (< 18.5)	797 (67)	46 (58)	
Normal weight (≥ 18.5 and < 25)	92 (8)	8 (10)	
Overweight (≥ 25 and < 30)	213 (18)	17 (22)	
Obese (≥ 30)	90 (8)	8 (10)	
Parity			0.05
No child	519 (44)	44 (56)	
One child or more	673 (56)	35 (44)	
Mother's fish consumption before pregnancy			0.08
Less than twice/week	924 (78)	54 (68)	
Twice/week or more	268 (22)	25 (32)	
Mother's tobacco consumption during pregnancy (n, % No)			0.30
No	942 (79)	58 (73)	
Yes	250 (21)	21 (27)	
Breastfeeding			0.49
Breastfed less than 6 months	886 (74)	62 (78)	
Breastfed 6 months or more	306 (26)	17 (22)	
Mode of day care at 24 months			0.38
Collective childcare facility	267 (22)	17 (22)	
Childminder or neighbor	699 (59)	42 (53)	
Family	226 (19)	20 (25)	
	Median (IQR)		
Mother's age at conception (Years)	29.7 (26.8, 32.7)	28.5 (25.9, 31.7)	0.07
Maternal stimulation at 24 months	4.3 (4.0, 5.0)	4.5 (4.0, 5.0)	0.59
HOME score at 5-6 years	0.2 (-0.5, 0.8)	0.2 (-0.4, 0.8)	0.81
Child age at the cognitive test (Years)	5.7 (5.6, 5.9)	5.7 (5.6, 6.0)	0.01
Deprivation index	-1.8 (-3.3, 0.0)	-1.3 (-2.9, 0.2)	0.12
PM ₁₀ concentration (µg/m ³) ^a	19.4 (18.3, 20.0)	18.7 (17.6, 19.6)	<0.001
PM _{2.5} concentration (µg/m ³) ^a	12.5 (11.7, 13.1)	12.0 (11.3, 12.6)	<0.001
NO ₂ concentration (µg/m ³) ^a	17.0 (15.6, 19.8)	15.8 (14.9, 17.6)	<0.001
General abilities	0.1 (-0.4, 0.6)	-0.1 (-0.6, 0.4)	0.11
Verbal abilities	0.2 (-0.9, 1.1)	-0.3 (-1.4, 0.7)	0.06
Non-verbal abilities	0.1 (-0.8, 1.0)	-0.2 (-1.1, 1.0)	0.39

Abbreviations: BMI: body mass index; IQR: InterQuartile Range

^a Average from the conception until the 60th month of life

^b Chi test for categorical variables and Wilcoxon test for continuous variables (because some variables not normally distributed)

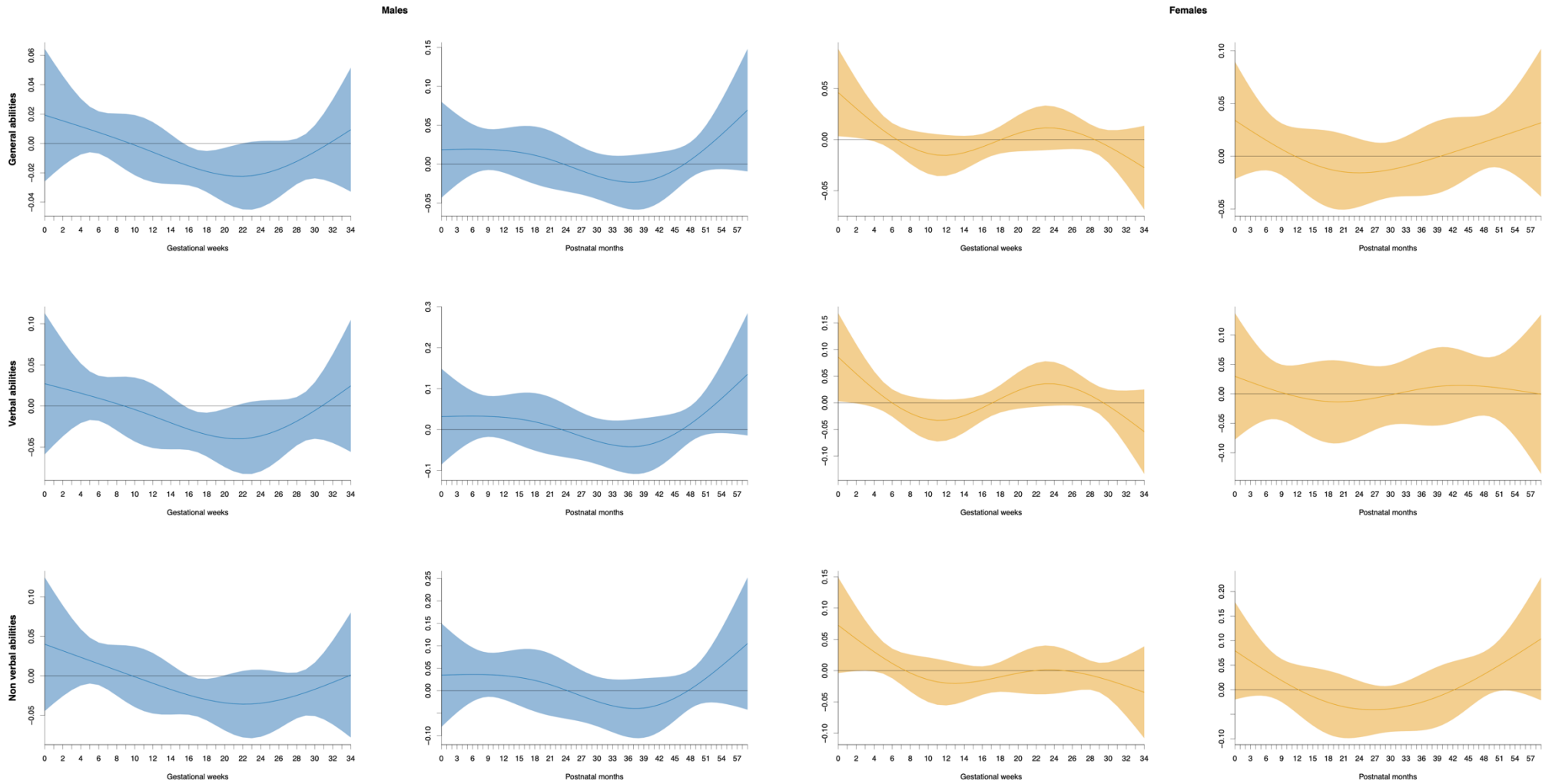


Figure S4: Sex-stratified lag-specific effect of a 10 µg/m³ increase in NO₂ concentration on children’s cognitive abilities - Main analyses

Shaded areas represent the 95% CI of the estimate.

Abbreviations: CI: Confidence Interval.

Models adjusted for the recruitment center, maternal education, maternal age at conception, maternal prepregnancy body mass index, maternal fish consumption before pregnancy, parity, child prenatal tobacco exposure, breastfeeding, child stimulation through maternal interactions, Home Observation Measurement of the Environment, method of child care, age at the cognitive test and the French European Deprivation Index.

n = 1271 mother-child pairs from the EDEN and PELAGIE cohorts.

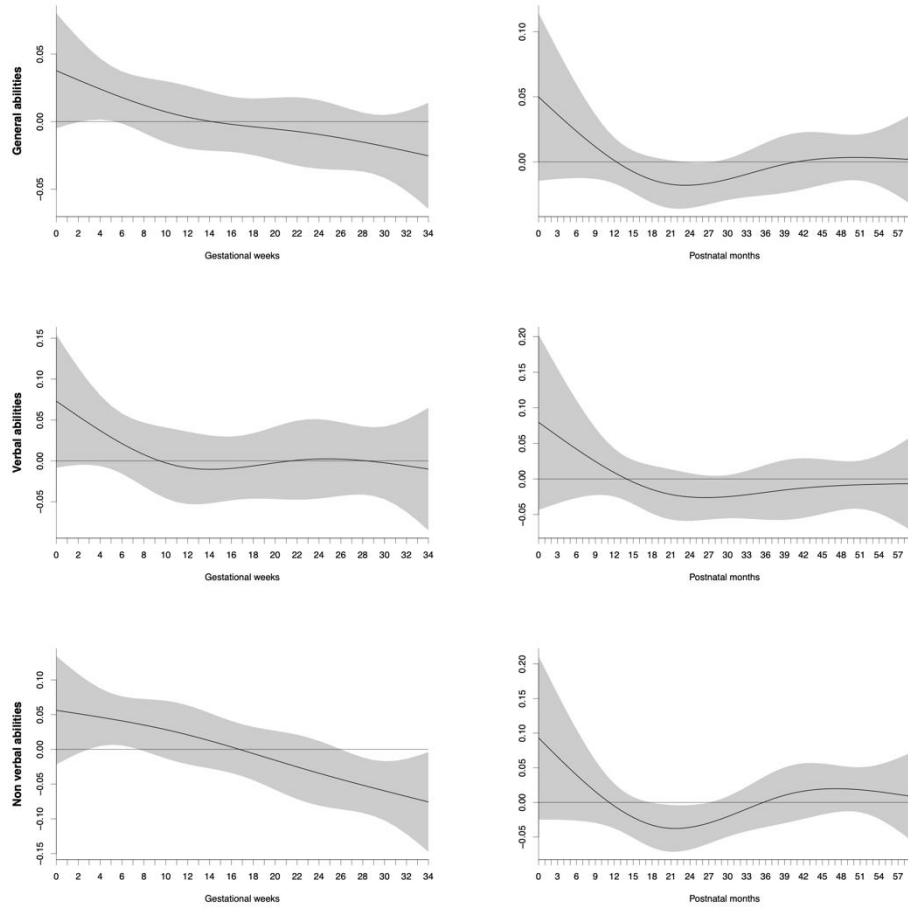


Figure S5: Non-sex stratified lag-specific effect of a 10 $\mu\text{g}/\text{m}^3$ increase in PM_{10} concentration on children's cognitive abilities - Main analyses

Shaded areas represent the 95% CI of the estimate.

Abbreviations: CI: Confidence Interval.

Models adjusted for the recruitment center, maternal education, maternal age at conception, maternal prepregnancy body mass index, maternal fish consumption before pregnancy, parity, child sex, child prenatal tobacco exposure, breastfeeding, child stimulation through maternal interactions, Home Observation Measurement of the Environment, method of child care, age at the cognitive test and the French European Deprivation Index.

n = 1271 mother-child pairs from the EDEN and PELAGIE cohorts.

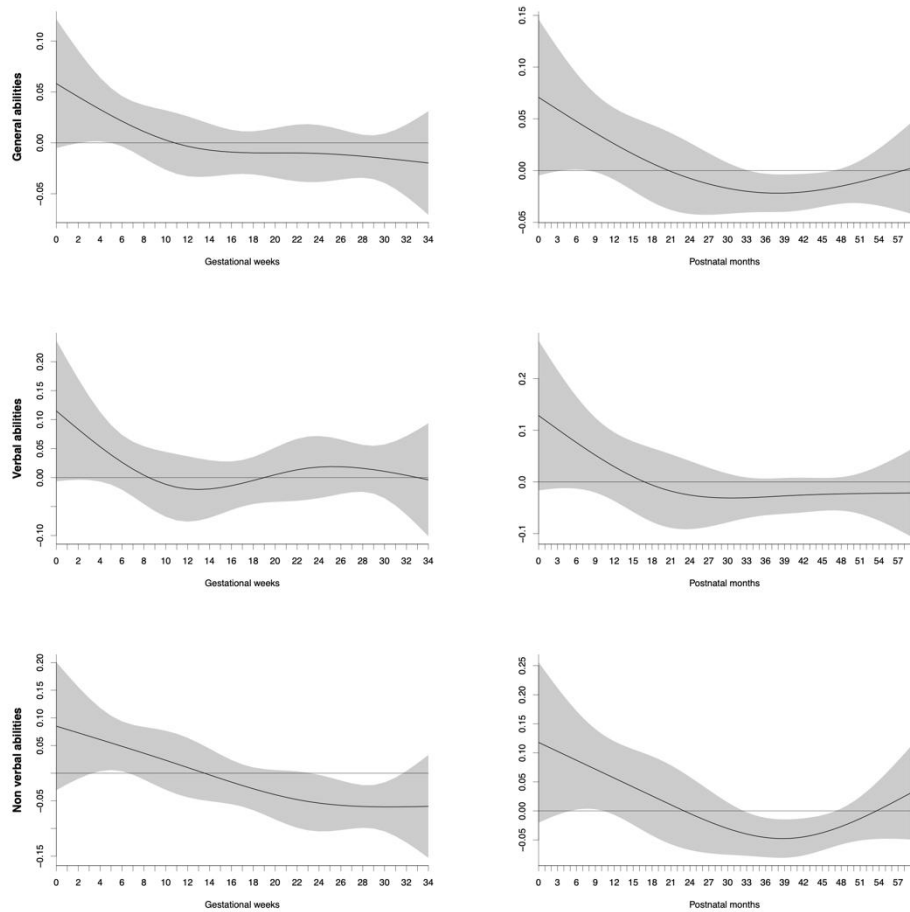


Figure S6: Non-sex stratified lag-specific effect of a 10 $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ concentration on children's cognitive abilities - Main analyses

Shaded areas represent the 95% CI of the estimate.

Abbreviations: CI: Confidence Interval.

Models adjusted for the recruitment center, maternal education, maternal age at conception, maternal prepregnancy body mass index, maternal fish consumption before pregnancy, parity, child sex, child prenatal tobacco exposure, breastfeeding, child stimulation through maternal interactions, Home Observation Measurement of the Environment, method of child care, age at the cognitive test and the French European Deprivation Index.

n = 1271 mother-child pairs from the EDEN and PELAGIE cohorts.

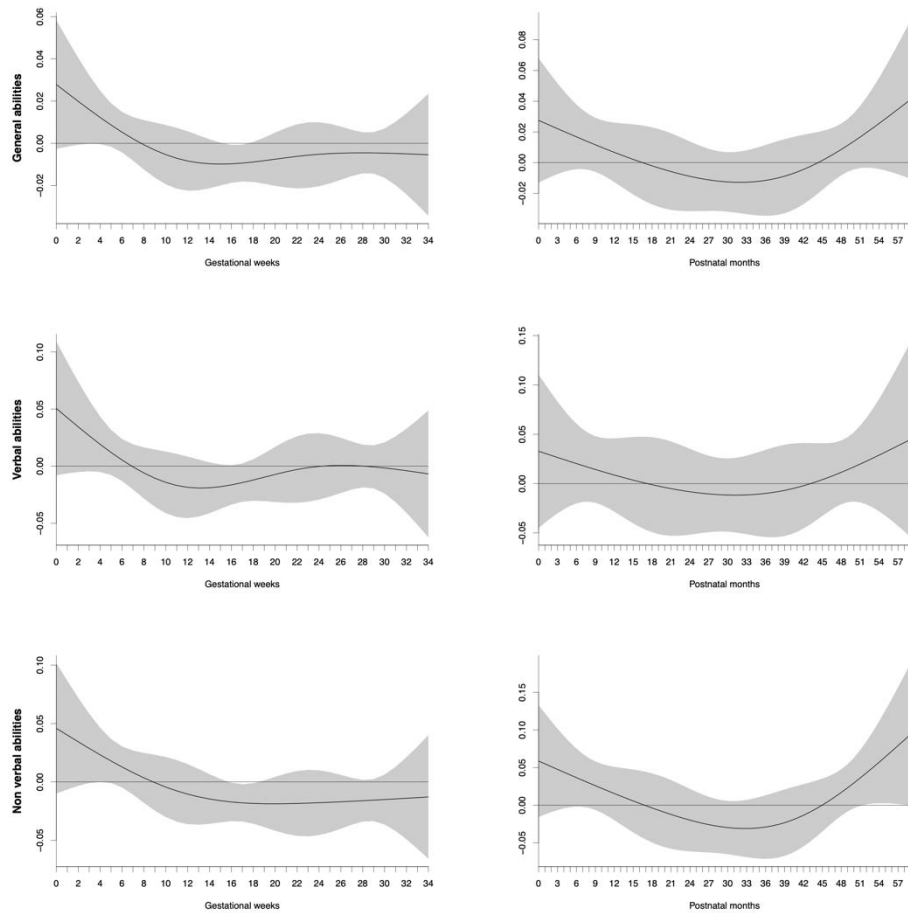


Figure S7: Non-sex stratified lag-specific effect of a 10 $\mu\text{g}/\text{m}^3$ increase in NO_2 concentration on children's cognitive abilities - Main analyses

Shaded areas represent the 95% CI of the estimate.

Abbreviations: CI: Confidence Interval.

Models adjusted for the recruitment center, maternal education, maternal age at conception, maternal prepregnancy body mass index, maternal fish consumption before pregnancy, parity, child sex, child prenatal tobacco exposure, breastfeeding, child stimulation through maternal interactions, Home Observation Measurement of the Environment, method of child care, age at the cognitive test and the French European Deprivation Index.

n = 1271 mother-child pairs from the EDEN and PELAGIE cohorts.

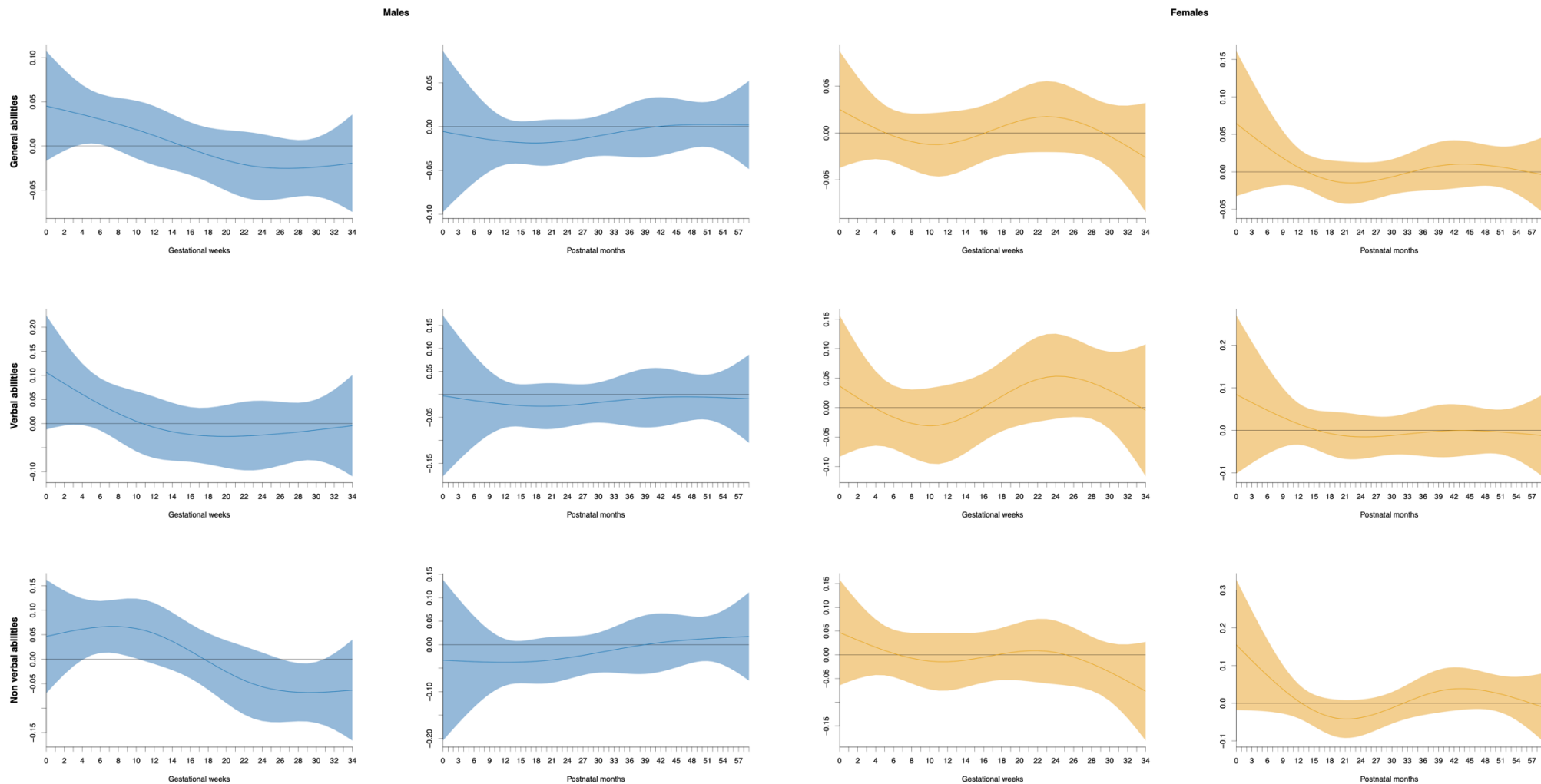


Figure S8: Sex-stratified lag-specific effect of a $10 \mu\text{g}/\text{m}^3$ increase in PM_{10} concentration on children's cognitive abilities - Sensitivity analyses

Shaded areas represent the 95% CI of the estimate.

Abbreviations: CI: Confidence Interval.

Models adjusted for the recruitment center, maternal education, maternal age at conception, maternal prepregnancy body mass index, maternal fish consumption before pregnancy, parity, child prenatal tobacco exposure, breastfeeding, child stimulation through maternal interactions, Home Observation Measurement of the Environment, method of child care, age at the cognitive test and the French European Deprivation Index.

n = 1192 mother-child pairs from the EDEN and PELAGIE cohorts.

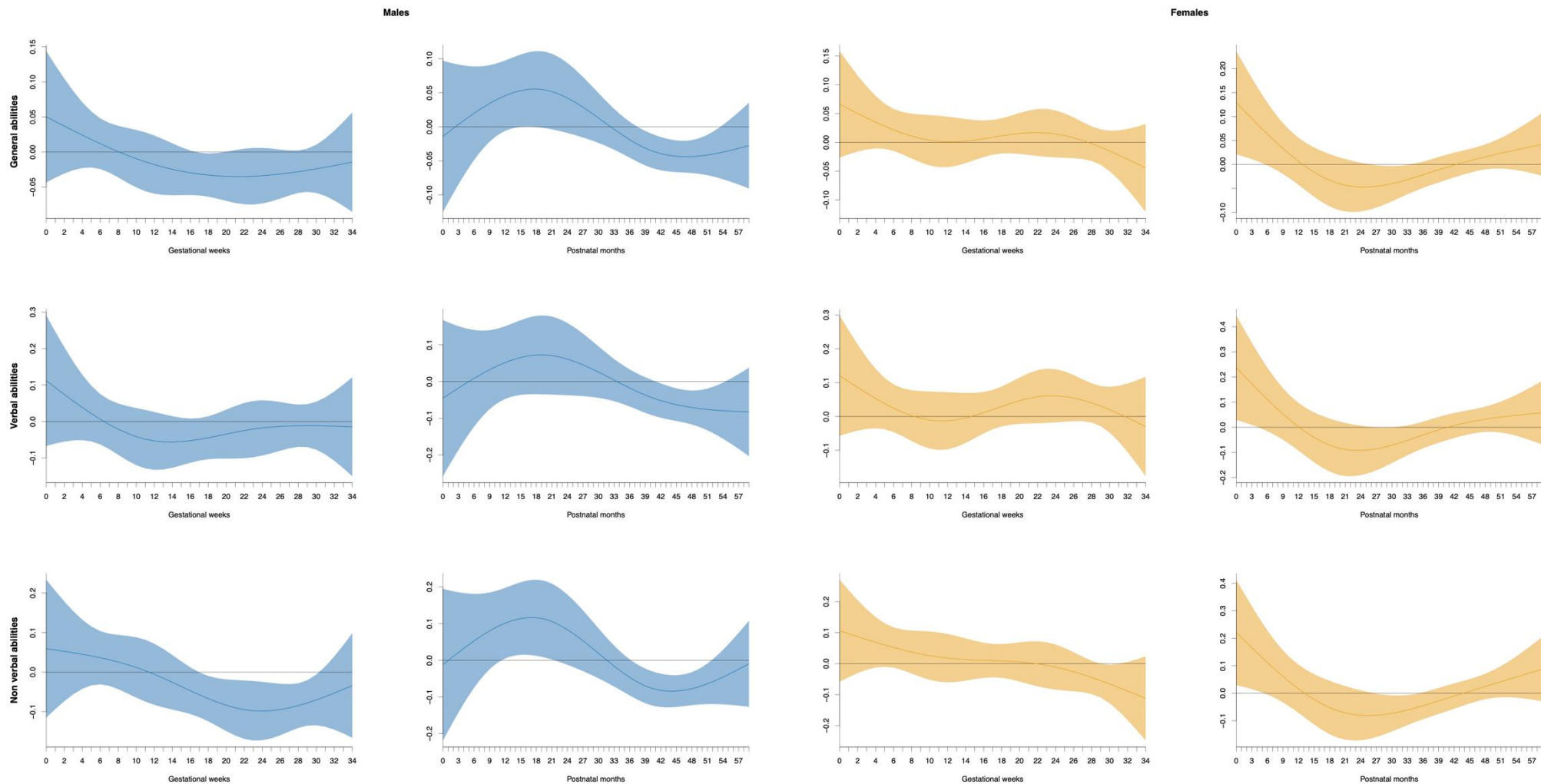


Figure S9: Sex-stratified lag-specific effect of a 10 $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ concentration on children's cognitive abilities - Sensitivity analyses

Shaded areas represent the 95% CI of the estimate.

Abbreviations: CI: Confidence Interval.

Models adjusted for the recruitment center, maternal education, maternal age at conception, maternal prepregnancy body mass index, maternal fish consumption before pregnancy, parity, child prenatal tobacco exposure, breastfeeding, child stimulation through maternal interactions, Home Observation Measurement of the Environment, method of child care, age at the cognitive test and the French European Deprivation Index.

n = 1192 mother-child pairs from the EDEN and PELAGIE cohorts.

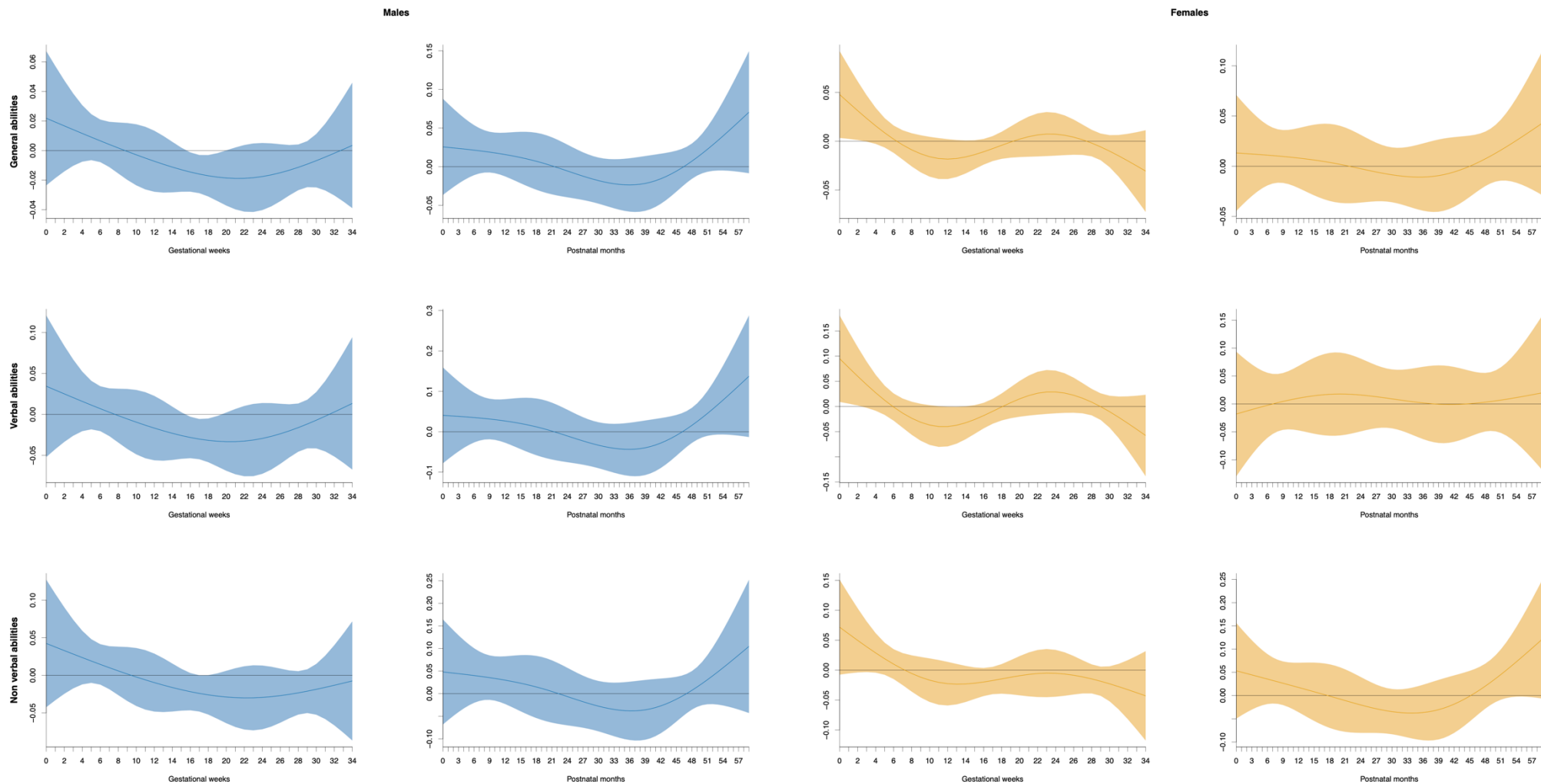


Figure S10: Sex-stratified lag-specific effect of a 10 µg/m³ increase in NO₂ concentration on children’s cognitive abilities - Sensitivity analyses

Shaded areas represent the 95% CI of the estimate.

Abbreviations: CI: Confidence Interval.

Models adjusted for the recruitment center, maternal education, maternal age at conception, maternal prepregnancy body mass index, maternal fish consumption before pregnancy, parity, child prenatal tobacco exposure, breastfeeding, child stimulation through maternal interactions, Home Observation Measurement of the Environment, method of child care, age at the cognitive test and the French European Deprivation Index.

n = 1192 mother-child pairs from the EDEN and PELAGIE cohorts.

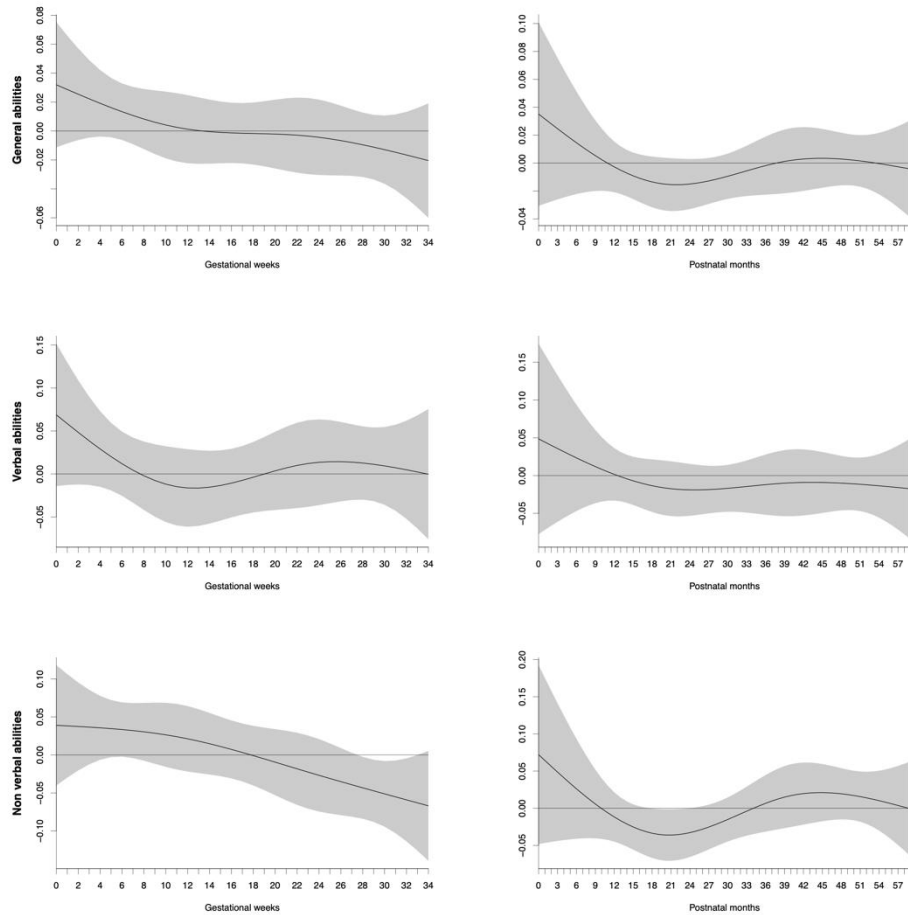


Figure S11: Non-sex stratified lag-specific effect of a $10 \mu\text{g}/\text{m}^3$ increase in PM_{10} concentration on children's cognitive abilities - Sensitivity analyses

Shaded areas represent the 95% CI of the estimate.

Abbreviations: CI: Confidence Interval.

Models adjusted for the recruitment center, maternal education, maternal age at conception, maternal prepregnancy body mass index, maternal fish consumption before pregnancy, parity, child sex, child prenatal tobacco exposure, breastfeeding, child stimulation through maternal interactions, Home Observation Measurement of the Environment, method of child care, age at the cognitive test and the French European Deprivation Index.

n = 1192 mother-child pairs from the EDEN and PELAGIE cohorts.

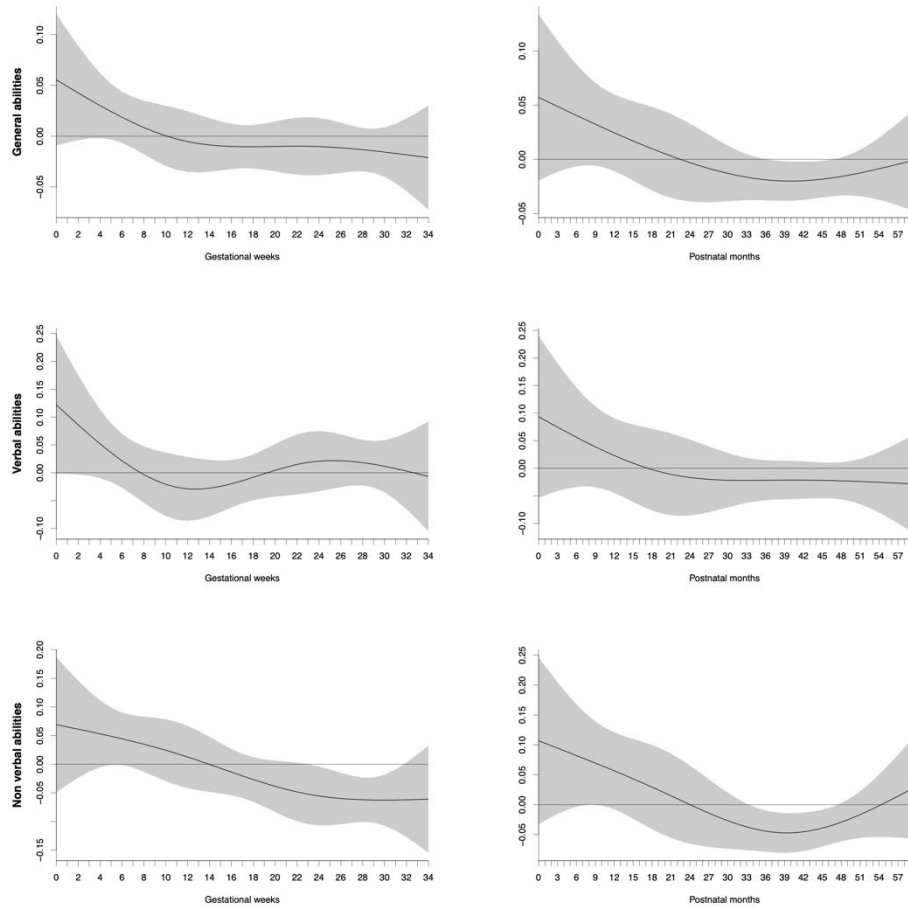


Figure S12: Non-sex stratified lag-specific effect of a 10 $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ concentration on children's cognitive abilities - Sensitivity analyses

Shaded areas represent the 95% CI of the estimate.

Abbreviations: CI: Confidence Interval.

Models adjusted for the recruitment center, maternal education, maternal age at conception, maternal prepregnancy body mass index, maternal fish consumption before pregnancy, parity, child sex, child prenatal tobacco exposure, breastfeeding, child stimulation through maternal interactions, Home Observation Measurement of the Environment, method of child care, age at the cognitive test and the French European Deprivation Index.

n = 1192 mother-child pairs from the EDEN and PELAGIE cohorts.

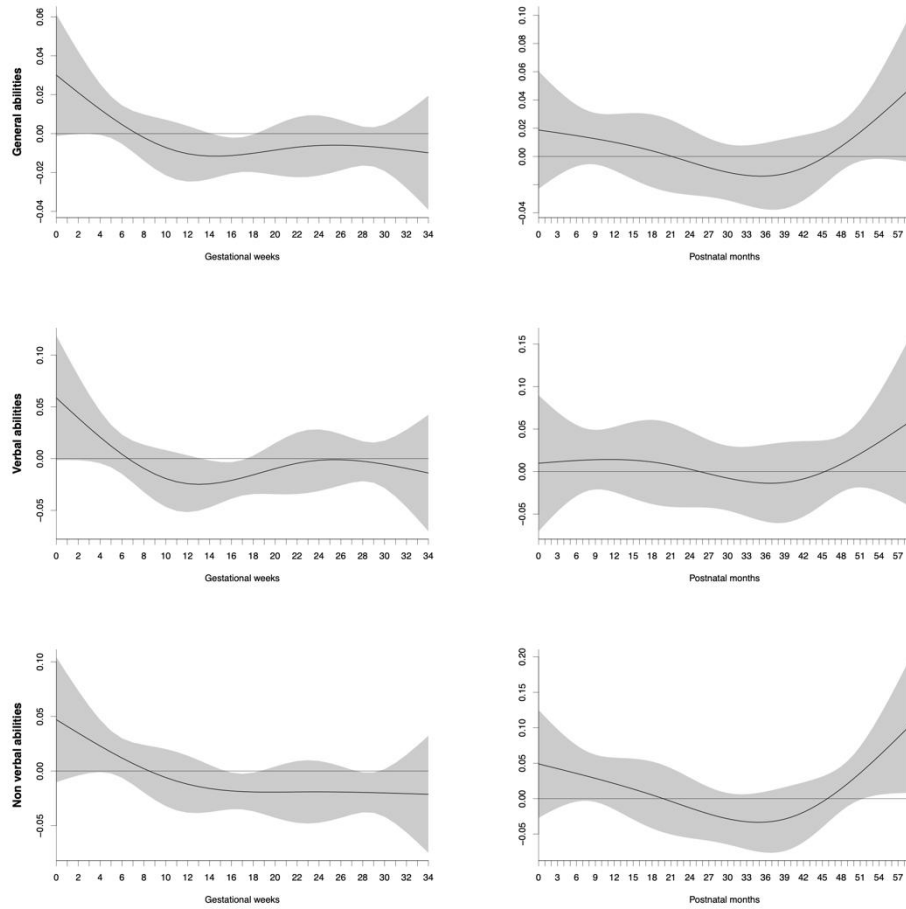


Figure S13: Non-sex stratified lag-specific effect of a 10 $\mu\text{g}/\text{m}^3$ increase in NO_2 concentration on children's cognitive abilities - Sensitivity analyses

Shaded areas represent the 95% CI of the estimate.

Abbreviations: CI: Confidence Interval.

Models adjusted for the recruitment center, maternal education, maternal age at conception, maternal prepregnancy body mass index, maternal fish consumption before pregnancy, parity, child sex, child prenatal tobacco exposure, breastfeeding, child stimulation through maternal interactions, Home Observation Measurement of the Environment, method of child care, age at the cognitive test and the French European Deprivation Index.

n = 1192 mother-child pairs from the EDEN and PELAGIE cohorts.