Prenatal exposure to non-persistent chemical mixtures and offspring IQ and emotional and behavioral problems

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Table S1. Descriptive statistics of biomarker concentrations included in the analyses by weeks of gestation [a]

		Min	P10	P20	P25	P50	P75	P80	P90	Max	% below LOD
Phthalate metabolites											
Monomethyl (MMP)											
	<18 weeks	0.2	1.5	2.2	2.6	5.1	9.4	10.9	17.1	505.9	0.3
	18-25 weeks	0.1	1.2	1.8	2.0	3.9	7.0	8.0	12.3	2446.9	0.1
	>25 weeks	0.1	1.2	1.8	2.1	4.1	8.2	9.3	15.8	1059.8	0.5
Monoethyl (MEP)											
	<18 weeks	1.3	14.3	28.9	36.3	121.1	443.5	603.8	1214.8	9482.7	0.1
	18-25 weeks	1.5	10.5	23.6	29.1	85.7	274.0	362.8	725.3	10214.4	0.0
	>25 weeks	1.4	17.0	32.0	40.7	123.8	407.4	534.6	1180.9	10799.8	0.0
Mono-n-butyl (MnBP)											
	<18 weeks	0.3	3.2	5.7	7.4	17.3	33.7	40.3	64.8	2715.6	0.6
	18-25 weeks	0.2	2.9	4.3	5.2	10.4	20.5	23.9	39.3	265.9	0.0
	>25 weeks	0.2	2.8	4.4	5.3	10.4	20.7	25.2	42.7	2573.4	0.3
Mono-isobutyl (MiBP)											
	<18 weeks	0.3	5.1	8.2	9.8	22.2	46.0	55.0	92.1	1826.6	0.3
	18-25 weeks	0.5	2.8	4.3	5.2	10.4	20.4	24.7	43.0	1733.0	0.0
	>25 weeks	0.8	4.1	6.5	7.7	13.8	30.4	37.4	70.9	2057.1	0.1
Mono-(2-ethyl-5-carboxypentyl) (MECPP)											
	<18 weeks	0.4	4.1	6.7	8.1	15.9	30.6	36.0	60.2	906.1	0.3
	18-25 weeks	0.5	2.9	4.9	5.8	10.9	20.1	23.2	35.3	93301.2	0.1
	>25 weeks	0.5	5.3	7.8	9.3	17.5	33.1	41.2	65.7	451.4	0.0
Mono-(2-ethyl-5-hydroxyhexyl) (MEHHP)											
	<18 weeks	0.1	2.2	4.5	5.4	11.6	22.3	26.4	42.0	827.2	0.3
	18-25 weeks	0.4	1.7	2.6	3.2	6.2	12.9	15.8	22.1	184.1	0.1
	>25 weeks	0.1	2.5	3.9	4.5	9.6	18.9	22.2	35.7	336.9	0.3
Mono-(2-ethyl-5oxohexyl) (MEOHP)											
	<18 weeks	0.1	1.4	2.9	3.4	7.8	15.9	19.3	31.7	613.9	0.0
	18-25 weeks	0.5	2.3	3.4	4.1	9.4	20.4	23.6	35.5	11831.0	0.0
	>25 weeks	0.4	2.0	2.7	3.1	6.1	12.9	14.4	22.3	167.7	0.1
Mono-[(2-carboxymethyl)hexyl] (MCMHP)											
	<18 weeks	0.3	3.9	5.9	7.0	13.4	24.8	28.4	44.1	893.9	0.1
	18-25 weeks	0.1	1.2	2.1	2.4	4.4	7.8	9.0	13.8	5497.2	0.4
	>25 weeks	0.1	1.0	1.6	1.9	3.6	6.6	7.6	10.7	352.0	1.2
Mono(3-carboxypropyl) (MCPP)											
	<18 weeks	0.0	0.4	0.6	0.7	1.3	2.5	2.8	4.4	120.2	0.0
	18-25 weeks	0.1	0.3	0.5	0.5	0.9	1.7	2.0	3.1	63.1	0.0
	>25 weeks	0.1	0.5	0.9	1.0	1.8	3.0	3.4	5.6	60.4	0.1
Monobenzyl (MBzP)											
	<18 weeks	0.1	1.4	2.5	3.1	6.3	12.4	14.6	21.9	554.8	13.8
	18-25 weeks	0.2	1.1	1.8	2.2	5.5	10.7	13.1	25.4	522.9	0.8
	>25 weeks	0.2	0.5	0.7	1.0	2.4	4.6	5.5	9.2	128.0	3.6
Phthalic acid (PA)											
	<18 weeks	1.3	17.2	28.8	32.8	57.5	125.4	153.6	254.3	9450.0	0.4
	18-25 weeks	6.0	38.4	56.3	64.8	170.3	299.7	329.0	418.5	2189.3	0.1
	>25 weeks	1.5	17.9	28.3	33.1	66.3	129.8	153.0	245.0	1770.0	0.4
Bisphenols											
Bisphenol A (BPA)											
	<18 weeks	0.1	0.4	0.6	0.7	1.7	3.5	4.3	6.8	90.2	26.0
	18-25 weeks	0.2	0.5	0.7	0.9	1.7	3.4	4.0	7.2	109.5	6.7
	>25 weeks	0.2	0.4	0.6	0.8	1.6	3.0	3.8	6.0	64.9	13.3
Dialkylphosphate (DAP) metabolites											
dimethyldithiophosphate (DMDTP)											
	<18 weeks	0.1	0.2	0.2	0.2	0.5	1.1	1.4	2.8	75.6	19.9
	18-25 weeks	0.1	0.2	0.2	0.3	0.5	1.1	1.5	2.6	33.5	18.2
	>25 weeks	0.1	0.1	0.2	0.2	0.4	1.0	1.4	2.6	38.0	17.9
dimethylthiophosphate (DMTP)											
	<18 weeks	0.5	2.5	4.3	5.3	11.2	21.8	28.2	45.3	343.2	3.5
	18-25 weeks	0.4	2.6	4.6	5.6	12.3	23.7	27.3	42.2	489.0	3.6
	>25 weeks	0.4	2.7	4.5	5.6	11.3	22.1	26.3	41.7	284.9	2.4
dimethylphosphate (DMP)											
	<18 weeks	0.5	3.5	5.5	6.6	12.2	22.9	27.1	40.1	209.1	0.1
	18-25 weeks	0.6	3.4	5.4	6.6	12.2	21.3	24.9	33.7	289.3	0.0
	>25 weeks	0.6	3.4	5.2	6.1	11.5	21.2	24.1	39.6	200.3	0.0
diethylthiophosphate (DETP)											
	<18 weeks	0.1	0.3	0.5	0.5	1.3	2.9	3.7	6.8	117.2	12.2
	18-25 weeks	0.1	0.3	0.4	0.4	1.0	2.4	2.9	5.2	99.9	11.9
	>25 weeks	0.1	0.3	0.4	0.5	1.1	2.8	3.3	5.6	64.9	11.9
Diethylphosphate (DEP)											
	<18 weeks	0.5	1.0	1.6	1.9	3.8	7.2	8.4	13.8	1035.7	2.7
	18-25 weeks	0.5	1.0	1.5	1.8	3.5	6.6	7.8	12.4	168.5	5.4
	>25 weeks	0.5	1.1	1.6	1.8	3.7	7.4	8.5	13.7	77.5	4.1

Abbreviations: Min = Minimum, P = percentile, % = percentage, LOD = limit of detection.
a. Descriptive statistics of concentrations for individual biomarkers are in ng/mL in which the concentrations below the LOD are excluded.

Table S2. Descriptive statistics of biomarker concentrations excluded from the analyses [a]

	Min	P25	P50	P75	Max	% below LOD
Phthalate metabolites						
Mono isononyl (MiNP)						
<18 weeks	0.1	0.3	0.5	1.3	16.1	86.8
18-25 weeks	0.2	0.2	0.2	0.4	0.6	97.8
>25 weeks	-	-	-	-	-	100.0
Monocyclohexyl (MCHP)						
<18 weeks	0.0	0.1	0.1	0.3	6.4	85.4
18-25 weeks	0.0	0.0	0.1	0.1	1.4	91.0
>25 weeks	0.2	0.3	0.4	1.3	2.2	99.4
Monooctyl (MOP)						
<18 weeks	0.3	0.3	0.5	0.8	9.3	90.0
18-25 weeks	0.4	0.5	0.5	0.5	0.6	99.5
>25 weeks	0.3	0.4	0.4	0.7	1.7	99.1
Mono-(8-methyl-1-nonyl) (MiDP)						
<18 weeks	0.9	1.3	1.8	2.6	14.2	88.6
18-25 weeks	1.0	1.1	1.2	1.5	4.7	97.3
>25 weeks	0.9	2.3	2.9	5.1	15.1	95.9
Mono-hexyl (MHxP)						
<18 weeks	0.0	0.2	0.3	0.6	59.9	32.8
18-25 weeks	0.1	0.1	0.1	0.1	0.4	98.6
>25 weeks	0.0	0.4	0.6	0.7	2.1	97.8
Mono-2-heptyl (MHpP)						
<18 weeks	0.2	0.6	1.0	1.9	78.7	44.4
18-25 weeks	0.3	0.4	0.6	0.7	1.3	94.9
>25 weeks	0.3	0.7	1.0	1.7	24.5	98.2
Mono-(7-carboxy-n-heptyl) (MCHpP)						
<18 weeks	0.1	0.1	0.1	0.1	0.2	98.6
18-25 weeks	-	-	-	-	-	100.0
>25 weeks	0.3	0.9	1.5	2.6	3.7	99.6
Bisphenols						
Bisphenol S						
<18 weeks	0.0	0.2	0.3	0.8	27.0	32.2
18-25 weeks	0.1	0.1	0.3	0.5	20.0	56.0
>25 weeks	0.1	0.3	0.6	1.4	16.7	78.2
Bisphenol F						
<18 weeks	0.2	0.3	0.7	1.6	82.7	65.0
18-25 weeks	0.2	0.3	0.5	1.2	14.3	85.3
>25 weeks	0.2	0.7	1.2	2.2	42.7	69.0
Bisphenol Z						
<18 weeks	0.1	0.2	0.2	0.5	2.3	90.8
18-25 weeks	0.1	0.1	0.2	0.2	0.4	93.7
>25 weeks	1.0	1.0	1.1	1.2	1.3	99.7
Bisphenol B						
<18 weeks	0.0	0.1	0.1	0.2	1.6	85.3
18-25 weeks	0.0	0.1	0.1	0.2	0.5	96.3
>25 weeks	-	-	-	-	-	100.0
Bisphenol AP						
<18 weeks	0.1	0.1	0.2	0.4	2.7	87.3
18-25 weeks	-	-	-	-	-	100.0
>25 weeks	0.2	0.2	0.2	0.2	0.2	99.9
Bisphenol AF						
<18 weeks	-	-	-	-	-	100.0
18-25 weeks	-	-	-	-	-	100.0
>25 weeks	3.7	3.7	3.7	3.7	3.7	99.9
Bisphenol P						
<18 weeks	0.1	0.1	0.2	0.3	1.8	97.1
18-25 weeks	-	-	-	-	-	100.0
>25 weeks	0.1	0.1	0.1	0.1	0.1	99.6
Dialkyl phosphate metabolites						
Diethyldithiophosphate (DEDTP)						
<18 weeks	0.1	0.1	0.1	0.2	34.0	81.1
18-25 weeks	0.1	0.1	0.1	0.2	5.2	84.5
>25 weeks	0.1	0.1	0.1	0.2	28.5	85.0

Abbreviations: Min = Minimum, P = percentile, % = percentage, LOD = limit of detection.
a. Descriptive statistics of concentrations for individual biomarkers are in ng/mL in which the concentrations below the LOD are excluded.

Table S3. Characteristics of included and excluded participants from the prenatally enrolled Generation R study cohort (*n*=8879)

	Distribution (*n*=782) [a]	Distribution (*n*=8097) [a]	P-value [b]
Maternal age (years)	31 (28, 34)	30 (26, 33)	<0.001
Missing, *n*	-	2	
Maternal ethnicity			<0.001
Dutch	57.7	48.0	
Other western	12.7	11.5	
Non-western	29.6	40.5	
Missing, *n*	-	501	
Maternal IQ	100 (90, 107)	95 (84, 107)	<0.001
Missing, *n*	19	3103	
Maternal education			<0.001
Low	14.8	28.4	
Intermediate	30.2	31.0	
High	55.0	40.5	
Missing, *n*	24	794	
Household income			<0.001
<1200€/month	12.6	21.7	
1200 – 2000€/month	16.5	18.8	
> 2000€/month	70.9	59.4	
Missing, *n*	101	2134	
Maternal psychopathology	0.13 (0.08, 0.33)	0.17 (0.08, 0.38)	<0.001
Missing, *n*	94	2135	
Maternal body mass index (kg/m^2)	22 (21, 25)	23 (21, 26)	0.255
Missing, *n*	97	1652	
Maternal parity			<0.001
0	62.3	54.9	
1	26.6	30.2	
≥2	11.1	14.9	
Missing, *n*	4	121	
Maternal marital status			<0.001
Married/ living with partner	89.8	84.7	
No partner	10.2	15.3	
Missing, *n*	29	808	
Maternal smoking during pregnancy			0.003
No smoking during pregnancy	77.2	72.3	
Until pregnancy recognized	8.9	8.7	
Continued during pregnancy	13.9	19.0	
Missing, *n*	63	1076	
Maternal alcohol consumption during pregnancy			<0.001
No consumption during pregnancy	36.7	49.2	
Until pregnancy recognized	17.5	12.8	
Continued occasionally	39.3	30.8	
Continued frequently	6.5	7.3	
Missing, *n*	40	932	
Child sex (female)	49.1	49.6	0.785
Missing, *n*	-	154	

a. Median (25th percentile, 75th percentile) for continuous variables and percentage for categorical variables.
b. P-value calculated using a chi-squared test for categorical characteristics and an independent t-test for continuous characteristics.

Table S4. Distributions of averaged chemical biomarker concentrations (ug/g creatinine) [a] across pregnancy (*n*=782)

	Min	P25	P50	P75	Max
Phthalate metabolites					
Monomethyl (MMP)	0.6	2.9	4.1	6.0	175.7
Monoethyl (MEP)	5.4	51.0	116.6	256.2	3022.0
Mono-n-butyl (MnBP)	1.0	7.7	12.1	18.2	103.4
Mono-isobutyl (MiBP)	1.1	9.5	14.3	24.8	170.9
Mono-(2-ethyl-5-carboxypentyl) (MECPP)	0.6	10.0	14.5	20.9	227.3
Mono-(2-ethyl-5-hydroxyhexyl) (MEHHP)	0.3	5.6	8.8	13.5	112.8
Mono-(2-ethyl-5oxohexyl) (MEOHP)	0.9	5.0	7.7	12.0	98.5
Mono-[(2-carboxymethyl)hexyl] (MCMHP)	0.1	4.2	5.7	7.9	105.2
Mono(3-carboxypropyl) (MCPP)	0.2	0.9	1.3	1.9	22.0
Monobenzyl (MBzP)	0.2	1.8	3.4	6.0	67.6
Phthalic acid (PA)	9.4	54.4	84.2	124.4	516.7
Bisphenols					
Bisphenol A (BPA)	0.1	0.7	1.1	1.8	27.6
Dialkylphosphate (DAP) metabolites					
dimethyldithiophosphate (DMDTP)	0.0	0.2	0.4	0.8	8.2
dimethylthiophosphate (DMTP)	0.0	8.9	14.8	22.4	103.0
dimethylphosphate (DMP)	2.0	11.9	16.5	23.0	76.5
diethylthiophosphate (DETP)	0.0	0.5	1.2	2.1	14.2
Diethylphosphate (DEP)	0.3	3.2	4.9	7.5	86.4

Abbreviations: Min = Minimum, P = percentile, LOD = limit of detection.

a. Phthalate and bisphenol concentration values below the LOD are imputed using the LOD/sqrt2. Lab reported machine DAP metabolite concentrations below the LOD used.

Table S5. Pearson and Spearman Rank correlation matrix of pregnancy averaged exposure biomarker concentrations.

Pearson correlations	MMP	MEP	MCPP	MiBP	MnBP	MECPP	MCMHP	MBzP	PA	MOEHP	MEHHP	BPA	DETP	DEP	DMDTP	DMTP
MMP	-															
MEP	0.15	-														
MCPP	0.22	0.03	-													
MiBP	0.17	0.05	0.35	-												
MnBP	0.19	0.10	0.47	0.57	-											
MECPP	0.24	0.03	0.52	0.39	0.42	-										
MCMHP	0.16	0.07	0.38	0.32	0.40	0.61	-									
MBzP	0.15	0.14	0.22	0.33	0.37	0.26	0.30	-								
PA	0.38	0.55	0.34	0.25	0.29	0.35	0.30	0.17								
MOEHP	0.21	0.00	0.53	0.53	0.58	0.76	0.63	0.30	0.34	-						
MEHHP	0.21	-0.02	0.52	0.49	0.56	0.74	0.65	0.24	0.31	0.90	-					
BPA	0.05	0.01	0.18	0.11	0.14	0.25	0.14	0.08	0.24	0.20	0.19	-				
DETP	0.06	-0.06	0.05	-0.02	-0.02	0.08	0.04	-0.10	0.00	0.07	0.08	0.09	-			
DEP	0.09	-0.05	0.00	-0.10	-0.01	0.00	0.05	-0.05	-0.02	0.04	0.06	-0.05	0.40	-		
DMDTP	0.01	-0.05	0.04	-0.06	-0.05	0.10	-0.02	-0.05	-0.04	0.04	0.05	0.11	0.53	0.16	-	
DMTP	0.03	-0.08	0.12	0.03	0.01	0.16	0.01	-0.03	0.00	0.14	0.14	0.07	0.63	0.22	0.70	-
DMP	0.09	-0.06	0.11	0.03	0.05	0.11	0.09	0.01	0.01	0.14	0.17	-0.05	0.25	0.60	0.25	0.36

Spearman Rank correlations	MMP	MEP	MCPP	MiBP	MnBP	MECPP	MCMHP	MBzP	PA	MOEHP	MEHHP	BPA	DETP	DEP	DMDTP	DMTP
MMP	-															
MEP	0.18	-														
MCPP	0.29	0.03	-													
MiBP	0.24	0.07	0.38	-												
MnBP	0.25	0.09	0.48	0.62	-											
MECPP	0.30	0.00	0.55	0.41	0.43	-										
MCMHP	0.22	0.06	0.39	0.36	0.41	0.59	-									
MBzP	0.19	0.12	0.22	0.35	0.39	0.25	0.31	-								
PA	0.38	0.54	0.33	0.26	0.29	0.34	0.30	0.15	-							
MOEHP	0.29	-0.02	0.54	0.54	0.57	0.77	0.63	0.30	0.32	-						
MEHHP	0.28	-0.04	0.53	0.51	0.56	0.75	0.64	0.25	0.29	0.92	-					
BPA	0.06	0.01	0.17	0.10	0.13	0.25	0.13	0.05	0.24	0.21	0.20	-				
DETP	0.09	-0.07	0.08	-0.02	0.00	0.12	0.07	-0.10	0.03	0.11	0.13	0.07	-			
DEP	0.12	-0.04	0.02	-0.08	0.00	0.02	0.07	-0.03	0.02	0.05	0.07	-0.04	0.47	-		
DMDTP	0.02	-0.04	0.03	-0.07	-0.05	0.12	0.00	-0.03	-0.02	0.05	0.05	0.10	0.49	0.19	-	
DMTP	0.06	-0.10	0.16	0.04	0.02	0.18	0.04	-0.05	0.01	0.17	0.17	0.06	0.61	0.34	0.72	-
DMP	0.10	-0.08	0.11	0.03	0.06	0.09	0.11	0.03	0.00	0.12	0.15	-0.05	0.31	0.61	0.29	0.52

See Table S1 for biomarker abbreviations and Figure 1 for a graphical presentation of the Pearson correlation matrix.

Table S6. Descriptive statistics of nonverbal IQ, internalizing problems, attention problems, aggressive behavior, and autistic traits

	Mean	SD
Nonverbal IQ (N=708)	102.3	15.4
Internalizing problems (N=773)	6.0	5.7
Attention problems (N=775)	1.6	1.8
Aggressive behavior (N=771)	6.3	5.6
Autistic traits (N=662)	0.2	0.2

Table S7. Adjusted [a] estimates for associations between mixtures of pregnancy averaged biomarker concentrations (ug/g creatinine) and nonverbal IQ, emotional and behavioral symptoms at the age of 6 years: model coefficients and differences relative to the lowest quartile of each mixture

	Nonverbal IQ (n=708)		Internalizing problems (n=773) [b]		Attention problems (n=775) [b]		Aggressive behavior (n=771) [b]		Autistic traits (n=622) [b]	
	B	95%CI	B	95%CI	B	95%CI	B	95%CI	B	95%CI
Overall										
Mixture	-5.23	-9.07, -1.40	0.25	-0.09, 0.58	0.12	-0.06, 0.31	0.31	-0.02, 0.63	-0.02	-0.06, 0.01
^2	1.23	0.18, 2.27	-0.08	-0.16, 0.00	-0.06	-0.11, 0.00	-0.11	-0.20, -0.02	-	-
Difference per quartile										
Q1-Q2	-4.00	-7.00, -1.00	0.17	-0.10, 0.44	0.06	-0.08, 0.21	0.20	-0.06, 0.46	-0.02	-0.06, 0.02
Q1-Q3	-5.54	-10.24, -0.85	0.18	-0.26, 0.61	0.02	-0.22, 0.26	0.17	-0.23, 0.58	-0.04	-0.12, 0.03
Q1-Q4	-4.63	-10.76, 1.51	0.02	-0.54, 0.59	-0.14	-0.49, 0.21	-0.07	-0.61, 0.46	-0.06	-0.18, 0.05
Phthalate metabolites [c]										
Mixture	-4.68	-8.44, -0.91	-0.02	-0.15, 0.11	0.17	0.00, 0.35	0.30	0.01, 0.59	-0.02	-0.04, 0.01
^2	1.24	0.19, 2.28	-	-	-0.06	-0.11, 0.00	-0.11	-0.20, -0.02	-	-
Difference per quartile										
Q1-Q2	-3.44	-6.33, -0.55	-0.02	-0.15, 0.11	0.12	-0.01, 0.25	0.19	-0.02, 0.41	-0.02	-0.04, 0.01
Q1-Q3	-4.41	-8.76, -0.05	-0.04	-0.31, 0.22	0.13	-0.07, 0.32	0.17	-0.14, 0.47	-0.03	-0.09, 0.02
Q1-Q4	-2.90	-8.35, 2.55	-0.06	-0.46, 0.34	0.02	-0.23, 0.27	-0.08	-0.45, 0.29	-0.05	-0.13, 0.03
Bisphenol [d]										
Mixture	0.42	-0.60, 1.45	-0.01	-0.08, 0.07	-0.04	-0.09, 0.01	-0.04	-0.12, 0.04	0.00	-0.02, 0.01
^2	-	-	-	-	-	-	-	-	-	-
Difference per quartile										
Q1-Q2	0.42	-0.63, 1.47	-0.01	-0.08, 0.07	-0.04	-0.09, 0.01	-0.04	-0.11, 0.03	0.00	-0.02, 0.01
Q1-Q3	0.84	-1.26, 2.95	-0.01	-0.17, 0.14	-0.08	-0.19, 0.02	-0.08	-0.22, 0.06	-0.01	-0.04, 0.02
Q1-Q4	1.26	-1.89, 4.42	-0.02	-0.25, 0.21	-0.13	-0.28, 0.03	-0.12	-0.33, 0.10	-0.01	-0.06, 0.04
OP pesticide metabolites [e]										
Mixture	-0.99	-2.44, 0.46	0.26	-0.02, 0.55	-0.03	-0.1, 0.04	0.03	-0.07, 0.14	0.00	-0.02, 0.02
^2	-	-	-0.08	-0.16, 0.01	-	-	-	-	-	-
Difference per quartile										
Q1-Q2	-0.99	-2.27, 0.29	0.19	-0.02, 0.39	-0.03	-0.11, 0.04	0.03	-0.08, 0.14	0.00	-0.03, 0.02
Q1-Q3	-1.98	-4.55, 0.58	0.22	-0.07, 0.50	-0.06	-0.22, 0.09	0.07	-0.15, 0.28	-0.01	-0.05, 0.04
Q1-Q4	-2.97	-6.82, 0.88	0.09	-0.23, 0.42	-0.10	-0.32, 0.13	0.10	-0.23, 0.43	-0.01	-0.08, 0.06

See Table S1 for biomarker abbreviations and Figure 2 for a graphical representation of quartile-specific differences for the overall mixture and each chemical group mixture.

a. Models adjusted for fetal sex (categorical), maternal age (continuous), pre-pregnancy weight (continuous), height (continuous), education level (categorical), ethnicity (categorical), income (categorical), marital status (categorical), parity (categorical), smoking (categorical), alcohol use (categorical), folic acid use (categorical), and child age at assessment (continuous).
b. Square root transformed and additionally adjusted for maternal psychopathology.
c. Models of the phthalate metabolite mixture (MMP, MEP, MCPP, MiBP, MnBP, MECPP, MCMHP, MBzP, PA, MEOHP, MEHHP) adjusted for covariates in the total mixtures model plus log 10-transformed pregnancy-averaged concentrations of bisphenol A (BPA) and OP pesticide metabolites (DMDTP, DMTP, DMP, DETP, DEP).
d. Models of the bisphenol mixture (BPA) adjusted for covariates in the total mixtures model plus log 10-transformed pregnancy-averaged concentrations of phthalate (MMP, MEP, MCPP, MiBP, MnBP, MECPP, MCMHP, MBzP, PA, MEOHP, MEHHP) and OP pesticide metabolites (DMDTP, DMTP, DMP, DETP, DEP).
e. Models of the OP pesticide metabolite mixture (DMDTP, DMTP, DMP, DETP, DEP) adjusted for covariates in the total mixtures model plus log 10-transformed pregnancy-averaged concentrations of phthalate metabolites (MMP, MEP, MCPP, MiBP, MnBP, MECPP, MCMHP, MBzP, PA, MEOHP, MEHHP) and bisphenol A.
^2: the inclusion of a quadratic term if improved model fit based on significantly lower Akaike information criteria (AIC): nonverbal IQ = MMP, internalizing problems = DETP, attention problems = MEHHP, aggressive behavior = MCPP.

Table S8. Adjusted [a] estimates for associations between mixtures of pregnancy averaged biomarker concentrations (ug/g creatinine) and externalizing problems at the age of 6 years: model coefficients and differences relative to the lowest quartile of each mixture

		Externalizing problems (*n*=776) [b]	
		B	95%CI
Overall			
	Mixture	0.31	-0.03, 0.65
	^2	-0.12	-0.22, -0.02
	Difference per quartile		
	Q1-Q2	0.19	-0.07, 0.45
	Q1-Q3	0.15	-0.25, 0.54
	Q1-Q4	-0.13	-0.65, 0.40
Phthalate metabolites [c]			
	Mixture	0.33	0.02, 0.65
	^2	-0.12	-0.22, -0.01
	Difference per quartile		
	Q1-Q2	0.22	-0.01, 0.45
	Q1-Q3	0.20	-0.12, 0.53
	Q1-Q4	-0.05	-0.48, 0.38
Bisphenol [d]			
	Mixture	-0.05	-0.13, 0.03
	^2	-	-
	Difference per quartile		
	Q1-Q2	-0.05	-0.13, 0.03
	Q1-Q3	-0.10	-0.25, 0.06
	Q1-Q4	-0.15	-0.38, 0.08
OP pesticide metabolites [e]			
	Mixture	0.01	-0.11, 0.12
	^2	-	-
	Difference per quartile		
	Q1-Q2	0.01	-0.11, 0.12
	Q1-Q3	0.02	-0.21, 0.25
	Q1-Q4	0.03	-0.32, 0.37

See Table S1 for biomarker abbreviations.

a. Models adjusted for fetal sex (categorical), maternal age (continuous), pre-pregnancy weight (continuous), height (continuous), education level (categorical), ethnicity (categorical), income (categorical), marital status (categorical), parity (categorical), smoking (categorical), alcohol use (categorical), folic acid use (categorical), and child age at assessment (continuous).
b. Square root transformed and additionally adjusted for maternal psychopathology.
c. Models of the phthalate metabolite mixture (MMP, MEP, MCPP, MiBP, MnBP, MECPP, MCMHP, MBzP, PA, MEOHP, MEHHP) adjusted for covariates in the total mixtures model plus log 10-transformed pregnancy-averaged concentrations of bisphenol A (BPA) and OP pesticide metabolites (DMDTP, DMTP, DMP, DETP, DEP).
d. Models of the bisphenol mixture (BPA) adjusted for covariates in the total mixtures model plus log 10-transformed pregnancy-averaged concentrations of phthalate (MMP, MEP, MCPP, MiBP, MnBP, MECPP, MCMHP, MBzP, PA, MEOHP, MEHHP) and OP pesticide metabolites (DMDTP, DMTP, DMP, DETP, DEP).
e. Models of the OP pesticide metabolite mixture (DMDTP, DMTP, DMP, DETP, DEP) adjusted for covariates in the total mixtures model plus log 10-transformed pregnancy-averaged concentrations of phthalate metabolites (MMP, MEP, MCPP, MiBP, MnBP, MECPP, MCMHP, MBzP, PA, MEOHP, MEHHP) and bisphenol A.
^2: the inclusion of a quadratic term if improved model fit based on significantly lower Akaike information criteria (AIC): Externalizing problems = MCPP.

Table S9. Adjusted [a] estimates for associations between mixtures of pregnancy averaged biomarker concentrations (ug/g creatinine) and nonverbal IQ, emotional and behavioral symptoms at the age of 6 years: differences relative to the lowest quartile of each mixture additionally adjusted for birth year

	Nonverbal IQ (*n*=708)		Internalizing problems (*n*=773) [b]		Attention problems (*n*=775) [b]		Aggressive behavior (*n*=771) [b]		Autistic traits (*n*=622) [b]	
	B	95%CI	B	95%CI	B	95%CI	B	95%CI	B	95%CI
Overall										
Difference per quartile										
Q1-Q2	-4.00	-7.00, -1.00	0.17	-0.10, 0.45	0.08	-0.06, 0.22	0.20	-0.06, 0.46	-0.02	-0.06, 0.02
Q1-Q3	-5.43	-10.13, -0.74	0.18	-0.26, 0.62	0.03	-0.21, 0.27	0.18	-0.23, 0.58	-0.04	-0.12, 0.03
Q1-Q4	-4.30	-10.44, 1.84	0.03	-0.54, 0.60	-0.14	-0.49, 0.21	-0.06	-0.59, 0.46	-0.06	-0.18, 0.05
Phthalate metabolites [c]										
Difference per quartile										
Q1-Q2	-3.53	-6.43, -0.62	-0.02	-0.15, 0.11	0.14	0.01, 0.27	0.20	-0.02, 0.41	-0.02	-0.04, 0.01
Q1-Q3	-4.47	-8.85, -0.09	-0.04	-0.31, 0.22	0.15	-0.04, 0.34	0.17	-0.14, 0.48	-0.03	-0.09, 0.02
Q1-Q4	-2.82	-8.30, 2.66	-0.06	-0.46, 0.34	0.04	-0.21, 0.29	-0.08	-0.45, 0.30	-0.05	-0.13, 0.03
Bisphenol [d]										
Difference per quartile										
Q1-Q2	0.42	-0.64, 1.47	-0.01	-0.08, 0.07	-0.04	-0.09, 0.01	-0.04	-0.11, 0.03	0.00	-0.02, 0.01
Q1-Q3	0.84	-1.28, 2.95	-0.02	-0.17, 0.14	-0.08	-0.19, 0.02	-0.08	-0.22, 0.06	-0.01	-0.04, 0.02
Q1-Q4	1.25	-1.91, 4.42	-0.02	-0.25, 0.21	-0.12	-0.28, 0.03	-0.12	-0.33, 0.10	-0.01	-0.06, 0.04
OP pesticide metabolites [e]										
Difference per quartile										
Q1-Q2	-0.90	-2.19, 0.39	0.19	-0.01, 0.40	-0.04	-0.12, 0.04	0.03	-0.07, 0.14	0.00	-0.03, 0.02
Q1-Q3	-1.80	-4.38, 0.78	0.23	-0.06, 0.51	-0.08	-0.23, 0.07	0.07	-0.15, 0.29	-0.01	-0.05, 0.04
Q1-Q4	-2.70	-6.57, 1.17	0.10	-0.22, 0.43	-0.12	-0.35, 0.11	0.10	-0.22, 0.43	-0.01	-0.08, 0.06

See Table S1 for biomarker abbreviations.

a. Models adjusted for fetal sex (categorical), maternal age (continuous), pre-pregnancy weight (continuous), height (continuous), education level (categorical), ethnicity (categorical), income (categorical), marital status (categorical), parity (categorical), smoking (categorical), alcohol use (categorical), folic acid use (categorical), child age at assessment (continuous), and birth year (continuous).
b. Square root transformed and additionally adjusted for maternal psychopathology.
c. Models of the phthalate metabolite mixture (MMP, MEP, MCPP, MiBP, MnBP, MECPP, MCMHP, MBzP, PA, MEOHP, MEHHP) adjusted for covariates in the total mixtures model plus log 10-transformed pregnancy-averaged concentrations of bisphenol A (BPA) and OP pesticide metabolites (DMDTP, DMTP, DMP, DETP, DEP).
d. Models of the bisphenol mixture (BPA) adjusted for covariates in the total mixtures model plus log 10-transformed pregnancy-averaged concentrations of phthalate (MMP, MEP, MCPP, MiBP, MnBP, MECPP, MCMHP, MBzP, PA, MEOHP, MEHHP) and OP pesticide metabolites (DMDTP, DMTP, DMP, DETP, DEP).
e. Models of the OP pesticide metabolite mixture (DMDTP, DMTP, DMP, DETP, DEP) adjusted for covariates in the total mixtures model plus log 10-transformed pregnancy-averaged concentrations of phthalate metabolites (MMP, MEP, MCPP, MiBP, MnBP, MECPP, MCMHP, MBzP, PA, MEOHP, MEHHP) and bisphenol A.
^2: the inclusion of a quadratic term if improved model fit based on significantly lower Akaike information criteria (AIC): nonverbal IQ = MMP, internalizing problems = DETP, attention problems = MEHHP, aggressive behavior = MCPP.

Table S10. Adjusted [a, b] estimates for associations between mixtures of pregnancy averaged biomarker concentrations (ug/g creatinine) and nonverbal IQ, emotional and behavioral symptoms at the age of 6 years: differences relative to the lowest quartile of each mixture stratified by sex

		Nonverbal IQ (*n*=708) [c]		Internalizing problems (*n*=773) [c, d]		Attention problems (*n*=775) [c, d]		Aggressive behavior (*n*=771) [c, d]		Autistic traits (*n*=622) [d]	
		B	95%CI	B	95%CI	B	95%CI	B	95%CI	B	95%CI
All classes											
	Q1-Q2	-4.00	-7.00, -1.00	.0.17	-0.10, 0.44	0.06	-0.08, 0.21	0.20	-0.06, 0.46	-0.02	-0.06, 0.02
	Q1-Q3	-5.54	-10.24, -0.85	0.18	-0.26, 0.61	0.02	-0.22, 0.26	0.17	-0.23, 0.58	-0.04	-0.12, 0.03
	Q1-Q4	-4.63	-10.76, 1.51	0.02	-0.54, 0.59	-0.14	-0.49, 0.21	-0.07	-0.61, 0.46	-0.06	-0.18, 0.05
Boys											
	Q1-Q2	-4.58	-9.66, 0.49	0.05	-0.32, 0.41	-0.01	-0.27, 0.26	0.03	-0.35, 0.41	-0.04	-0.09, 0.01
	Q1-Q3	-5.32	-13.11, 2.48	-0.02	-0.60, 0.56	-0.11	-0.54, 0.32	-0.18	-0.78, 0.41	-0.07	-0.17, 0.03
	Q1-Q4	-2.20	-11.98, 7.59	-0.21	-0.98, 0.57	-0.31	-0.88, 0.25	-0.64	-1.44, 0.15	-0.11	-0.26, 0.04
Girls											
	Q1-Q2	-4.61	-8.63, -0.58	0.25	-0.11, 0.62	0.18	-0.05, 0.41	0.34	0.01, 0.67	0.00	-0.05, 0.05
	Q1-Q3	-7.06	-13.74, -0.39	0.31	-0.30, 0.92	0.23	-0.13, 0.60	0.48	-0.06, 1.02	0.01	-0.09, 0.11
	Q1-Q4	-7.37	-16.92, 2.18	0.17	-0.70, 1.03	0.16	-0.34, 0.65	0.43	-0.31, 1.17	0.01	-0.14, 0.16
Phthalate metabolites [e]											
	Q1-Q2	-3.44	-6.33, -0.55	-0.02	-0.15, 0.11	0.12	-0.01, 0.25	0.19	-0.02, 0.41	-0.02	-0.04, 0.01
	Q1-Q3	-4.41	-8.76, -0.05	-0.04	-0.31, 0.22	0.13	-0.07, 0.32	0.17	-0.14, 0.47	-0.03	-0.09, 0.02
	Q1-Q4	-2.90	-8.35, 2.55	-0.06	-0.46, 0.34	0.02	-0.23, 0.27	-0.08	-0.45, 0.29	-0.05	-0.13, 0.03
Boys											
	Q1-Q2	-5.10	-9.75, -0.45	-0.06	-0.25, 0.14	0.06	-0.16, 0.27	0.17	-0.15, 0.48	-0.02	-0.06, 0.02
	Q1-Q3	-6.21	-12.94, 0.51	-0.11	-0.50, 0.28	0.01	-0.31, 0.32	0.07	-0.38, 0.53	-0.04	-0.12, 0.05
	Q1-Q4	-3.34	-11.29, 4.61	-0.17	-0.75, 0.42	-0.15	-0.55, 0.25	-0.28	-0.88, 0.33	-0.05	-0.18, 0.07
Girls											
	Q1-Q2	-3.34	-7.16, 0.49	-0.08	-0.29, 0.13	0.22	0.01, 0.44	0.21	-0.07, 0.49	0.00	-0.03, 0.04
	Q1-Q3	-4.46	-10.33, 1.41	-0.16	-0.57, 0.25	0.32	0.01, 0.62	0.22	-0.19, 0.63	0.01	-0.06, 0.08
	Q1-Q4	-3.38	-11.17, 4.40	-0.24	-0.86, 0.38	0.28	-0.08, 0.64	0.04	-0.48, 0.57	0.01	-0.10, 0.12
Bisphenol [f]											
	Q1-Q2	0.42	-0.63, 1.47	-0.01	-0.08, 0.07	-0.04	-0.09, 0.01	-0.04	-0.11, 0.03	0.00	-0.02, 0.01
	Q1-Q3	0.84	-1.26, 2.95	-0.01	-0.17, 0.14	-0.08	-0.19, 0.02	-0.08	-0.22, 0.06	-0.01	-0.04, 0.02
	Q1-Q4	1.26	-1.89, 4.42	-0.02	-0.25, 0.21	-0.13	-0.28, 0.03	-0.12	-0.33, 0.10	-0.01	-0.06, 0.04
Boys											
	Q1-Q2	0.61	-0.96, 2.17	-0.03	-0.14, 0.07	-0.07	-0.15, 0.00	-0.12	-0.22, -0.02	-0.02	-0.04, 0.00
	Q1-Q3	1.22	-1.92, 4.35	-0.07	-0.28, 0.14	-0.14	-0.29, 0.00	-0.24	-0.44, -0.04	-0.04	-0.08, 0.00
	Q1-Q4	1.83	-2.87, 6.52	-0.10	-0.41, 0.21	-0.22	-0.44, 0.00	-0.36	-0.66, -0.06	-0.06	-0.12, 0.01
Girls											
	Q1-Q2	-0.08	-1.54, 1.39	0.07	-0.05, 0.18	-0.01	-0.09, 0.07	0.07	-0.05, 0.18	0.00	-0.02, 0.03
	Q1-Q3	-0.15	-3.07, 2.77	0.14	-0.09, 0.37	-0.02	-0.17, 0.13	0.13	-0.10, 0.36	0.01	-0.04, 0.05
	Q1-Q4	-0.23	-4.61, 4.16	0.21	-0.14, 0.55	-0.03	-0.26, 0.20	0.20	-0.15, 0.54	0.01	-0.06, 0.08
OP pesticide metabolites [g]											
	Q1-Q2	-0.99	-2.27, 0.29	0.19	-0.02, 0.39	-0.03	-0.11, 0.04	0.03	-0.08, 0.14	0.00	-0.03, 0.02
	Q1-Q3	-1.98	-4.55, 0.58	0.22	-0.07, 0.50	-0.06	-0.22, 0.09	0.07	-0.15, 0.28	-0.01	-0.05, 0.04
	Q1-Q4	-2.97	-6.82, 0.88	0.09	-0.23, 0.42	-0.10	-0.32, 0.13	0.10	-0.23, 0.43	-0.01	-0.08, 0.06
Boys											
	Q1-Q2	-0.81	-2.91, 1.29	0.12	-0.18, 0.43	-0.01	-0.12, 0.11	-0.02	-0.19, 0.15	-0.01	-0.04, 0.03
	Q1-Q3	-1.62	-5.83, 2.58	0.14	-0.29, 0.56	-0.01	-0.25, 0.22	-0.03	-0.37, 0.31	-0.01	-0.07, 0.05
	Q1-Q4	-2.44	-8.74, 3.87	0.05	-0.45, 0.55	-0.02	-0.37, 0.33	-0.05	-0.56, 0.46	-0.02	-0.11, 0.08
Girls											

Q1-Q2	-0.99	-3.01, 1.04	0.24	-0.03, 0.52	-0.05	-0.16, 0.06	0.05	-0.13, 0.22	-0.01	-0.04, 0.02
Q1-Q3	-1.97	-6.01, 2.07	0.28	-0.09, 0.64	-0.10	-0.32, 0.11	0.10	-0.26, 0.45	-0.03	-0.08, 0.03
Q1-Q4	-2.96	-9.02, 3.11	0.10	-0.34, 0.54	-0.16	-0.48, 0.17	0.14	-0.38, 0.67	-0.04	-0.12, 0.05

See Table S1 for biomarker abbreviations.

a Models adjusted for fetal sex (categorical), maternal age (continuous), pre-pregnancy weight (continuous), height (continuous), education level (categorical), ethnicity (categorical), income (categorical), marital status (categorical), parity (categorical), smoking (categorical), alcohol use (categorical), folic acid use (categorical), and child age at assessment (continuous).

b. Sex stratified models adjusted for maternal age (continuous), pre-pregnancy weight (continuous), height (continuous), education level (categorical), ethnicity (categorical), income (categorical), marital status (categorical), parity (categorical), smoking (categorical), alcohol use (categorical), folic acid use (categorical), and child age at assessment (continuous).

c. The inclusion of a quadratic term if improved model fit based on significantly lower Akaike information criteria (AIC): nonverbal IQ = MMP, internalizing problems = DETP, attention problems = MEHHP, aggressive behavior = MCPP.

d. Square root transformed and additionally adjusted for maternal psychopathology.

e. Models of the phthalate metabolite mixture (MMP, MEP, MCPP, MiBP, MnBP, MECPP, MCMHP, MBzP, PA, MEOHP, MEHHP) adjusted for covariates in the total mixtures model plus log 10-transformed pregnancy-averaged concentrations of bisphenol A (BPA) and OP pesticide metabolites (DMDTP, DMTP, DMP, DETP, DEP).

f. Models of the bisphenol mixture (BPA) adjusted for covariates in the total mixtures model plus log 10-transformed pregnancy-averaged concentrations of phthalate (MMP, MEP, MCPP, MiBP, MnBP, MECPP, MCMHP, MBzP, PA, MEOHP, MEHHP) and OP pesticide metabolites (DMDTP, DMTP, DMP, DETP, DEP).

g. Models of the OP pesticide metabolite mixture (DMDTP, DMTP, DMP, DETP, DEP) adjusted for covariates in the total mixtures model plus log 10-transformed pregnancy-averaged concentrations of phthalate metabolites (MMP, MEP, MCPP, MiBP, MnBP, MECPP, MCMHP, MBzP, PA, MEOHP, MEHHP) and bisphenol A.