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Supplemental Material

Prenatal Exposure to Multiple Endocrine-Disrupting Chemicals and Childhood BMI Trajectories in the INMA Cohort Study

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Table S1: Details regarding laboratories and LOD or LOQ by sampling period for Gipuzkoa subcohort of the INMA birth cohort study

EDC		1 st trimester only			3 rd trimester only		Pooled (1 st + 3 rd)	
	Lab	LOD/Q	N	% <LOD/Q	N	% <LOD/Q	N	% <LOD/Q
Phthalates:								
MEP	NIPH	0.15	20	0%	5	0%	229	0%
MiBP	NIPH	0.15	20	0%	5	0%	229	0%
MnBP	NIPH	0.15	20	0%	5	0%	229	0%
MBzP	NIPH	0.06	20	0%	5	0%	228	0%
MEHP	NIPH	0.15	20	0%	5	0%	228	0%
MEHHP	NIPH	0.12	20	0%	5	0%	229	0%
MEOHP	NIPH	0.12	20	0%	5	0%	229	0%
MECPP	NIPH	0.61	20	0%	5	0%	229	0%
Phenols:								
MEPA	Granada	0.06	20	0%	6	0%	229	0%
ETPA	Granada	0.06	20	0%	6	0%	229	1.3%
PRPA	Granada	0.06	20	0%	6	0%	229	0%
BPA	Granada	0.12	20	20.0%	6	0%	229	19.7%
BUPA	Granada	0.04	20	25.0%	6	0%	229	10.0%
BP-3	Granada	0.07	20	5.0%	6	0%	229	3.1%
TRCS	not measured							
Organochlorine compounds:								
HCB	Gipuzkoa	0.071	549	9.3%				
DDE	Gipuzkoa	0.071	549	2.2%				
PFHxS	RWTH	0.2	324	7.4%				
PFOA	RWTH	0.2	324	0%				
PFOS	RWTH	0.2	324	0%				
PFNA	RWTH	0.1	324	0.3%				
Perfluoroalkyl substances:								
PCB 138	Gipuzkoa	0.071	548	6.8%				
PCB 153	Gipuzkoa	0.071	548	2.2%				
PCB 180	Gipuzkoa	0.071	549	3.6%				

Abbreviation: EDC = endocrine disrupting chemical, LOD/Q = limit of detection/quantification, N = number of observations, NIPH = Norwegian Institute of Public Health, RWTH = Rheinisch-Westfälische Technische Hochschule Aachen University

Table S2: Details regarding laboratories and LOD or LOQ by sampling period for Sabadell subcohort of the INMA birth cohort study

EDC		1 st trimester only			3 rd trimester only		Pooled (1 st + 3 rd)	
	Lab	LOD/Q	N	% <LOD/Q	N	% <LOD/Q	N	% <LOD/Q
Phthalates:								
MEP	IMIM	1	395	0%	403	0.2%		
MiBP	IMIM	0.5	395	0%	403	0%		
MnBP	IMIM	1	395	0.8%	403	0.5%		
MBzP	IMIM	0.5	395	0.8%	403	0.7%		
MEHP	IMIM	1	395	0.5%	403	0.5%		
MEHHP	IMIM	0.5	395	0%	403	0%		
MEOHP	IMIM	0.5	395	0%	403	0%		
MECPP	IMIM	1	395	0%	403	0.2%		
Phenols:								
MEPA	NIPH	0.03	99	0%	456	0%		
ETPA	NIPH	0.03	99	0%	456	0.7%		
PRPA	NIPH	0.03	99	1.0%	454	0.2%		
BPA	NIPH	0.03	99	0%	455	0.9%		
BUPA	NIPH	0.06	99	5.1%	454	5.1%		
BP-3	NIPH	0.03	99	0.0%	456	0%		
TRCS	NIPH	0.03	99	0.0%	456	0%		
Organochlorine compounds:								
HCB	Gipuzkoa	0.071	548	8.4%				
DDE	Gipuzkoa	0.071	548	0.2%				
PFHxS	RWTH	0.2	407	2.2%				
PFOA	RWTH	0.2	407	0%				
PFOS	RWTH	0.2	407	0%				
PFNA	RWTH	0.1	407	0.7%				
Perfluoroalkyl substances:								
PCB 138	Gipuzkoa	0.071	548	22.1%				
PCB 153	Gipuzkoa	0.071	548	7.8%				
PCB 180	Gipuzkoa	0.071	548	16.6%				
Abbreviation: EDC = endocrine disrupting chemical, IMIM = Hospital de Mar Medical Research Institute, LOD/Q = limit of detection/quantification, N = number of observations, NIPH = Norwegian Institute of Public Health, RWTH = Rheinisch-Westfälische Technische Hochschule Aachen University								

Table S3: Details regarding laboratories and LOD or LOQ by sampling period for Valencia subcohort of the INMA birth cohort study

EDC		1 st trimester only			3 rd trimester only		Pooled (1 st + 3 rd)	
	Lab	LOD/Q	N	% <LOD/Q	N	% <LOD/Q	N	% <LOD/Q
Phthalates:								
MEP	NIPH	0.15	6	0%	45	0%	270	0%
MiBP	NIPH	0.15	6	0%	45	0%	270	0%
MnBP	NIPH	0.15	6	0%	45	0%	270	0%
MBzP	NIPH	0.06	6	0%	45	0%	270	0%
MEHP	NIPH	0.15	6	0%	44	0%	270	0%
MEHHP	NIPH	0.12	6	0%	45	0%	270	0%
MEOHP	NIPH	0.12	6	0%	45	0%	270	0%
MECPP	NIPH	0.61	6	0%	45	0%	270	0%
Phenols:								
MEPA	NIPH	0.03	437	0%	437	0%		
ETPA	NIPH	0.03	437	0%	437	0%		
PRPA	NIPH	0.03	437	1.1%	437	0.5%		
BPA	NIPH	0.03	437	0%	437	0%		
BUPA	NIPH	0.07	437	10.3%	437	11.0%		
BP-3	NIPH	0.03	437	0%	437	0%		
TRCS	NIPH	0.07	437	0%	437	0%		
Organochlorine compounds:								
HCB	CSIC	0.029	598	5.5%				
DDE	CSIC	0.015	598	0.3%				
PFHxS	RWTH	0.2	505	2.6%				
PFOA	RWTH	0.2	505	0%				
PFOS	RWTH	0.2	505	0%				
PFNA	RWTH	0.1	505	0.8%				
Perfluoroalkyl substances:								
PCB 138	CSIC	0.028	598	4.0%				
PCB 153	CSIC	0.017	598	3.8%				
PCB 180	CSIC	0.015	598	2.8%				

Abbreviation: CSIC = Superior Council of Scientific Investigations, EDC = endocrine disrupting chemical, LOD/Q = limit of detection/quantification, N = number of observations, NIPH = Norwegian Institute of Public Health, RWTH = Rheinisch-Westfälische Technische Hochschule Aachen University

Table S4. Description of the growth trajectory modeling used in the INMA birth cohort study

Software used: RStudio 4.0.3 (RStudio Team (2020). RStudio: Integrated Development for R. RStudio, PBC, Boston, MA URL <http://www.rstudio.com/>.)

Package used: *lcmm*: Extended Mixed Models Using Latent Classes and Latent Processes

Objective: Find the different growth patterns using only the age of each measurement as a predictor.

Model parameters:

```
lcmm(fixed = zBMI ~ bs(age, df = 3), mixture = ~bs(age,  
      df = 3), subject = "id", ng = g, link = "linear", data = x)
```

Statistical Model:

Number of latent classes: 5

Goodness-of-fit statistics:

AIC: 66732.94

BIC: 66876.93

Table S5. Characteristics of the study population, unimputed and imputed data for the INMA birth cohort study			
Characteristic	Missing	Unimputed Data	Imputed Data
	(N)	N (%) or Mean (SD)	% or Mean (SD)
Sub-cohort	0		
Gipuzkoa		556 (29.1)	-
Sabadell		659 (34.5)	-
Valencia		696 (36.4)	-
Social Class	94		
High		594 (32.7)	32.6
Middle		477 (26.2)	26.3
Low		746 (41.1)	41.2
Smoking during pregnancy	33		
None		1293 (68.9)	68.9
Yes		585 (31.1)	31.1
Parity	96		
0		1012 (55.8)	55.4
1+		803 (44.2)	44.6
Maternal age (at delivery)	2	31.8 (4.2)	31.8 (4.2)
Maternal prepregnancy BMI	17	23.5 (4.2)	23.5 (4.3)
Paternal BMI (pregnancy)	112	25.8 (3.4)	25.8 (3.4)
Maternal Mediterranean diet score	94	8.0 (2.7)	8.0 (2.7)
Child sex	0		
Females		927 (48.5)	-
Males		984 (51.5)	-
Abbreviations: N = number of observations, SD = standard deviation, BMI = body mass index			

Table S6. Associations between EDCs and childhood BMI trajectories from single exposure models using multinomial regression models and expressed as relative risk ratios, for the INMA birth cohort study.

	Class 1 Higher birth size – accelerated BMI gain	Class 2 Higher birth size – slower BMI gain	Class 3 Lower birth size – accelerated BMI gain	Class 5 Lower birth size – slower BMI gain
	N = 212	N = 513	N = 292	N = 287
EDC	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)
MEP	1.05 (0.91, 1.20)	1.01 (0.92, 1.11)	0.99 (0.89, 1.11)	1.02 (0.91, 1.15)
MiBP	1.05 (0.84, 1.30)	1.02 (0.87, 1.19)	0.96 (0.80, 1.15)	0.98 (0.82, 1.17)
MnBP	1.00 (0.84, 1.20)	0.94 (0.83, 1.07)	0.96 (0.82, 1.12)	0.95 (0.82, 1.10)
MBzP	1.04 (0.86, 1.25)	1.04 (0.91, 1.19)	1.11 (0.94, 1.30)	1.00 (0.86, 1.17)
MEHP	1.08 (0.89, 1.33)	1.06 (0.93, 1.21)	1.08 (0.92, 1.27)	1.08 (0.92, 1.26)
MEHHP	1.13 (0.93, 1.37)	1.13 (0.97, 1.31)	1.08 (0.91, 1.29)	1.07 (0.90, 1.27)
MEOHP	1.14 (0.93, 1.39)	1.12 (0.96, 1.31)	1.08 (0.91, 1.29)	1.05 (0.89, 1.25)
MECPP	1.07 (0.86, 1.33)	1.07 (0.91, 1.27)	1.00 (0.83, 1.21)	1.03 (0.86, 1.24)
MEPA	0.98 (0.90, 1.07)	1.00 (0.93, 1.07)	0.99 (0.92, 1.07)	0.97 (0.90, 1.06)
ETPA	0.99 (0.91, 1.07)	0.98 (0.92, 1.04)	1.02 (0.95, 1.09)	1.03 (0.96, 1.10)
PRPA	1.00 (0.93, 1.07)	1.01 (0.95, 1.08)	1.02 (0.95, 1.08)	0.99 (0.93, 1.06)
BPA	1.02 (0.91, 1.14)	1.03 (0.95, 1.11)	1.01 (0.93, 1.10)	1.01 (0.90, 1.12)
BUPA	0.98 (0.92, 1.05)	1.00 (0.95, 1.06)	1.02 (0.96, 1.08)	0.99 (0.93, 1.05)
BP-3	1.00 (0.93, 1.07)	1.00 (0.95, 1.06)	1.01 (0.95, 1.08)	1.05 (0.99, 1.11)
TRCS ^a	1.02 (0.93, 1.10)	1.02 (0.96, 1.09)	0.98 (0.92, 1.05)	1.01 (0.94, 1.09)
HCB	1.17 (1.01, 1.36)	1.06 (0.96, 1.18)	1.25 (1.09, 1.42)	1.05 (0.93, 1.19)
DDE	1.15 (1.00, 1.32)	1.01 (0.91, 1.13)	1.19 (1.05, 1.35)	1.01 (0.90, 1.15)
PFHxS	0.77 (0.58, 1.01)	0.90 (0.75, 1.08)	1.14 (0.92, 1.43)	1.05 (0.84, 1.30)
PFOA	1.01 (0.76, 1.33)	1.02 (0.84, 1.24)	1.16 (0.92, 1.48)	1.05 (0.84, 1.33)
PFOS	0.93 (0.68, 1.26)	1.02 (0.81, 1.28)	1.25 (0.97, 1.61)	1.02 (0.80, 1.29)
PFNA	1.01 (0.76, 1.33)	1.11 (0.90, 1.36)	1.32 (1.05, 1.66)	1.08 (0.85, 1.36)
PCB 138	1.06 (0.89, 1.27)	1.05 (0.92, 1.20)	1.24 (1.05, 1.46)	1.07 (0.91, 1.24)
PCB 153	1.02 (0.85, 1.21)	0.98 (0.86, 1.12)	1.25 (1.05, 1.48)	1.01 (0.87, 1.17)
PCB 180	0.99 (0.82, 1.19)	1.03 (0.89, 1.19)	1.20 (1.01, 1.43)	1.06 (0.91, 1.25)

Reference outcome category is Class 4: average birth size and subsequent slower BMI gain (N = 607)

Using imputed data (m=20)

Abbreviations: BMI = body mass index, RRR = relative risk ratio, CI = confidence interval

^a TRCS only included two cohorts (Sabadell, Valencia) as such sample size was smaller (n = 1,355)

All models adjusted for sub-cohort, social class, smoking during pregnancy, parity, maternal age at delivery, maternal prepregnancy BMI, paternal prepregnancy BMI, maternal Mediterranean diet score, child sex.

Table S7. Associations between EDCs and childhood BMI trajectories from single exposure models using multinomial regression models and expressed as relative risk ratios for the INMA birth cohort study, complete case analysis.

EDC	N	Class 1	Class 2	Class 3	Class 5
		Higher birth size – accelerated BMI gain	Higher birth size – slower BMI gain	Lower birth size – accelerated BMI gain	Lower birth size – slower BMI gain
		RRR (95% CI)	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)
MEP	958	1.10 (0.94, 1.28)	1.01 (0.90, 1.13)	0.95 (0.83, 1.08)	0.99 (0.85, 1.14)
MiBP	958	1.09 (0.87, 1.36)	0.99 (0.83, 1.17)	0.96 (0.79, 1.16)	0.96 (0.79, 1.18)
MnBP	958	1.03 (0.87, 1.22)	0.89 (0.77, 1.02)	0.94 (0.81, 1.09)	0.91 (0.78, 1.07)
MBzP	957	1.05 (0.85, 1.28)	0.99 (0.85, 1.16)	1.19 (1.00, 1.40)	0.93 (0.78, 1.12)
MEHP	956	1.17 (0.94, 1.45)	1.05 (0.89, 1.24)	1.20 (1.00, 1.44)	1.02 (0.83, 1.25)
MEHHP	958	1.19 (0.95, 1.50)	1.13 (0.95, 1.35)	1.18 (0.97, 1.43)	0.98 (0.79, 1.23)
MEOHP	958	1.21 (0.95, 1.54)	1.13 (0.94, 1.36)	1.20 (0.98, 1.47)	0.97 (0.77, 1.22)
MECPP	958	1.10 (0.85, 1.42)	1.06 (0.88, 1.29)	1.04 (0.83, 1.29)	0.93 (0.73, 1.19)
MEPA	1121	0.98 (0.89, 1.08)	1.00 (0.93, 1.07)	0.99 (0.92, 1.08)	0.97 (0.89, 1.06)
ETPA	1121	1.01 (0.93, 1.10)	0.98 (0.92, 1.05)	1.03 (0.95, 1.10)	1.05 (0.97, 1.13)
PRPA	1119	1.01 (0.93, 1.09)	1.02 (0.96, 1.09)	1.03 (0.96, 1.11)	1.01 (0.94, 1.09)
BPA	1120	1.03 (0.92, 1.15)	1.04 (0.96, 1.12)	1.00 (0.91, 1.09)	0.98 (0.88, 1.08)
BUPA	1119	0.98 (0.91, 1.06)	1.00 (0.95, 1.06)	1.04 (0.97, 1.11)	0.98 (0.92, 1.05)
BP-3	1121	1.01 (0.94, 1.08)	1.01 (0.96, 1.06)	1.02 (0.96, 1.09)	1.05 (0.98, 1.11)
TRCS ^a	880	1.02 (0.93, 1.11)	1.03 (0.97, 1.10)	0.99 (0.91, 1.06)	1.03 (0.95, 1.11)
HCB	1649	1.19 (1.03, 1.39)	1.05 (0.95, 1.17)	1.24 (1.08, 1.41)	1.04 (0.92, 1.17)
DDE	1649	1.19 (1.03, 1.37)	1.01 (0.90, 1.12)	1.24 (1.09, 1.40)	1.06 (0.93, 1.20)
PFHxS	1205	0.82 (0.62, 1.08)	0.96 (0.77, 1.18)	1.27 (0.99, 1.64)	1.01 (0.79, 1.30)
PFOA	1205	1.18 (0.88, 1.59)	1.10 (0.88, 1.37)	1.29 (1.00, 1.65)	1.09 (0.84, 1.42)
PFOS	1205	0.98 (0.73, 1.33)	1.09 (0.87, 1.38)	1.33 (1.02, 1.74)	1.05 (0.80, 1.37)
PFNA	1205	1.08 (0.82, 1.43)	1.22 (0.98, 1.52)	1.50 (1.17, 1.92)	1.11 (0.86, 1.43)
PCB 138	1648	1.06 (0.88, 1.27)	1.05 (0.92, 1.21)	1.24 (1.05, 1.47)	1.06 (0.91, 1.25)
PCB 153	1648	1.02 (0.85, 1.22)	0.98 (0.86, 1.12)	1.24 (1.04, 1.48)	1.00 (0.86, 1.16)
PCB 180	1649	0.99 (0.82, 1.19)	1.03 (0.90, 1.19)	1.20 (1.00, 1.43)	1.04 (0.88, 1.23)

Reference outcome category is Class 4: average birth size and subsequent slower BMI gain

Abbreviations: BMI = body mass index, RRR = relative risk ratio, CI = confidence interval

^a TRCS only included two cohorts (Sabadell, Valencia) as such sample size was smaller (n = 1,355)

All models adjusted for sub-cohort, social class, smoking during pregnancy, parity, maternal age at delivery, maternal prepregnancy BMI, paternal prepregnancy BMI, maternal Mediterranean diet score, child sex.

Table S8. Associations between EDCs and childhood BMI trajectories from single exposure models using multinomial regression models and expressed as relative risk ratios for the INMA birth cohort study, by sex [females (n = 927) / males (n = 984)]

		Class 1 Higher birth size – accelerated BMI gain	Class 2 Higher birth size – slower BMI gain	Class 3 Lower birth size – accelerated BMI gain	Class 5 Lower birth size – slower BMI gain
Sex					
Females		N = 85 (40.1%)	N = 242 (47.2%)	N = 143 (49%)	N = 131 (45.6%)
Males		N = 127 (59.9%)	N = 271 (52.8%)	N = 149 (51%)	N = 156 (54.4%)
EDC		RRR (95% CI)	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)
MEP	Females	1.03 (0.83, 1.29)	1.01 (0.89, 1.15)	1.02 (0.87, 1.19)	1.05 (0.88, 1.25)
	Males	1.06 (0.90, 1.25)	1.02 (0.88, 1.17)	0.97 (0.83, 1.13)	0.99 (0.84, 1.18)
MiBP	Females	1.02 (0.75, 1.39)	1.06 (0.84, 1.34)	0.95 (0.74, 1.21)	0.97 (0.76, 1.25)
	Males	1.08 (0.82, 1.43)	0.99 (0.80, 1.22)	0.98 (0.77, 1.25)	0.99 (0.76, 1.28)
MnBP	Females	1.04 (0.79, 1.36)	0.91 (0.76, 1.09)	0.95 (0.78, 1.15)	0.94 (0.77, 1.14)
	Males	0.98 (0.79, 1.22)	0.97 (0.82, 1.15)	0.97 (0.79, 1.18)	0.96 (0.78, 1.19)
MBzP	Females	1.11 (0.83, 1.47)	1.07 (0.87, 1.32)	1.11 (0.89, 1.40)	0.95 (0.76, 1.18)
	Males	1.00 (0.79, 1.25)	1.01 (0.85, 1.21)	1.10 (0.90, 1.35)	1.04 (0.82, 1.31)
MEHP	Females	1.17 (0.89, 1.54)	1.11 (0.93, 1.34)	1.15 (0.93, 1.43)	1.10 (0.88, 1.37)
	Males	1.02 (0.79, 1.33)	1.02 (0.82, 1.26)	1.02 (0.81, 1.29)	1.06 (0.85, 1.31)
MEHHP	Females	1.29 (0.96, 1.73)	1.23 (1.01, 1.51)	1.21 (0.95, 1.52)	1.13 (0.88, 1.46)
	Males	1.01 (0.77, 1.31)	1.03 (0.82, 1.29)	0.96 (0.73, 1.25)	1.01 (0.8, 1.27)
MEOHP	Females	1.26 (0.95, 1.68)	1.21 (0.99, 1.48)	1.20 (0.95, 1.51)	1.13 (0.88, 1.46)
	Males	1.03 (0.78, 1.36)	1.04 (0.82, 1.31)	0.97 (0.73, 1.28)	0.98 (0.77, 1.23)
MECPP	Females	1.14 (0.81, 1.61)	1.15 (0.92, 1.44)	1.14 (0.88, 1.48)	1.10 (0.83, 1.45)
	Males	1.00 (0.75, 1.35)	1.00 (0.78, 1.28)	0.87 (0.65, 1.16)	0.97 (0.75, 1.25)
MEPA	Females	0.97 (0.85, 1.10)	0.99 (0.90, 1.09)	1.01 (0.91, 1.13)	0.94 (0.84, 1.06)
	Males	1.00 (0.89, 1.13)	1.00 (0.92, 1.09)	0.98 (0.88, 1.10)	1.00 (0.91, 1.11)
ETPA	Females	1.00 (0.89, 1.11)	1.00 (0.92, 1.08)	1.03 (0.93, 1.14)	1.03 (0.93, 1.14)
	Males	0.98 (0.89, 1.09)	0.96 (0.88, 1.05)	1.00 (0.91, 1.10)	1.02 (0.93, 1.13)
PRPA	Females	0.98 (0.88, 1.09)	1.01 (0.93, 1.09)	1.03 (0.94, 1.13)	0.96 (0.87, 1.06)
	Males	1.02 (0.92, 1.14)	1.02 (0.94, 1.11)	1.01 (0.91, 1.11)	1.03 (0.93, 1.14)
BPA	Females	1.03 (0.89, 1.18)	1.07 (0.96, 1.20)	1.06 (0.94, 1.20)	1.03 (0.89, 1.19)
	Males	1.00 (0.86, 1.15)	0.99 (0.90, 1.09)	0.96 (0.85, 1.08)	0.98 (0.85, 1.13)
BUPA	Females	1.02 (0.92, 1.14)	1.01 (0.94, 1.09)	1.05 (0.96, 1.14)	1.00 (0.91, 1.10)
	Males	0.95 (0.87, 1.03)	0.99 (0.92, 1.06)	1.00 (0.92, 1.08)	0.98 (0.90, 1.06)
BP-3	Females	1.03 (0.92, 1.15)	1.01 (0.94, 1.08)	1.00 (0.92, 1.09)	1.05 (0.97, 1.15)
	Males	0.97 (0.89, 1.07)	0.99 (0.92, 1.07)	1.02 (0.94, 1.11)	1.04 (0.97, 1.12)
TRCS ^a	Females	1.07 (0.93, 1.23)	1.06 (0.96, 1.16)	1.03 (0.93, 1.15)	1.06 (0.96, 1.18)
	Males	0.98 (0.88, 1.09)	0.99 (0.90, 1.08)	0.94 (0.85, 1.04)	0.96 (0.87, 1.08)
HCB	Females	1.21 (0.96, 1.52)	1.08 (0.92, 1.27)	1.23 (1.01, 1.49)	0.96 (0.81, 1.14)
	Males	1.17 (0.96, 1.41)	1.05 (0.91, 1.20)	1.27 (1.06, 1.52)	1.14 (0.96, 1.34)
DDE	Females	1.09 (0.87, 1.36)	0.95 (0.81, 1.11)	1.08 (0.89, 1.30)	1.01 (0.84, 1.20)
	Males	1.21 (1.01, 1.46)	1.08 (0.93, 1.26)	1.30 (1.10, 1.54)	1.03 (0.86, 1.22)

PFHxS	Females	0.75 (0.51, 1.11)	0.94 (0.72, 1.23)	1.29 (0.92, 1.82)	1.13 (0.81, 1.57)
	Males	0.76 (0.54, 1.06)	0.86 (0.67, 1.09)	1.02 (0.77, 1.35)	0.97 (0.73, 1.28)
PFOA	Females	1.04 (0.69, 1.56)	1.12 (0.85, 1.47)	1.24 (0.87, 1.78)	1.21 (0.87, 1.68)
	Males	0.95 (0.68, 1.33)	0.92 (0.70, 1.21)	1.06 (0.78, 1.45)	0.91 (0.65, 1.26)
PFOS	Females	0.85 (0.54, 1.34)	1.07 (0.77, 1.49)	1.26 (0.85, 1.88)	1.06 (0.75, 1.52)
	Males	0.97 (0.65, 1.44)	0.97 (0.72, 1.31)	1.24 (0.89, 1.72)	0.97 (0.70, 1.33)
PFNA	Females	0.99 (0.67, 1.45)	1.20 (0.89, 1.61)	1.28 (0.91, 1.79)	1.27 (0.93, 1.74)
	Males	0.99 (0.69, 1.43)	1.02 (0.78, 1.33)	1.35 (0.99, 1.86)	0.92 (0.66, 1.27)
PCB 138	Females	1.18 (0.89, 1.55)	1.08 (0.89, 1.33)	1.26 (0.98, 1.61)	1.12 (0.88, 1.42)
	Males	0.98 (0.78, 1.24)	1.03 (0.86, 1.23)	1.21 (0.97, 1.50)	1.02 (0.83, 1.26)
PCB 153	Females	1.02 (0.76, 1.36)	0.95 (0.77, 1.17)	1.21 (0.93, 1.58)	0.98 (0.77, 1.24)
	Males	1.02 (0.82, 1.27)	1.01 (0.86, 1.20)	1.26 (1.00, 1.59)	1.03 (0.85, 1.25)
PCB 180	Females	1.00 (0.75, 1.32)	1.03 (0.83, 1.27)	1.18 (0.91, 1.53)	1.04 (0.82, 1.31)
	Males	0.98 (0.77, 1.25)	1.04 (0.87, 1.26)	1.21 (0.95, 1.54)	1.09 (0.87, 1.36)
<p>Reference outcome category is Class 4: average birth size and subsequent slower BMI gain (Females: N = 326 (53.7%) / Males: N = 281 (46.3%))</p> <p>Using imputed data (m=20)</p> <p>Abbreviations: BMI = body mass index, RRR = relative risk ratio, CI = confidence interval</p> <p>^a TRCS only included two cohorts (Sabadell, Valencia) as such sample size was smaller (n = 647 for females, n = 708 for males).</p> <p>All models adjusted for sub-cohort, social class, smoking during pregnancy, parity, maternal age at delivery, maternal prepregnancy BMI, paternal prepregnancy BMI, maternal Mediterranean diet score.</p>					

Table S9. Associations between EDCs and childhood BMI growth trajectory classes from single exposure models for the INMA birth cohort study by socioeconomic status, high (n = 613) / middle (n = 497) / low (n = 777)

		Class 1	Class 2	Class 3	Class 5
SES		Higher birth size – accelerated BMI gain	Higher birth size – slower BMI gain	Lower birth size – accelerated BMI gain	Lower birth size – slower BMI gain
	High	N = 23.6%	N = 31.7%	N = 34.6%	N = 34.3%
	Middle	N = 28.5%	N = 26.6%	N = 23.8%	N = 24.9%
	Low	N = 47.9%	N = 41.7%	N = 41.6%	N = 40.8%
EDC		RRR (95% CI)	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)
MEP	High	1.14 (0.89, 1.48)	1.04 (0.89, 1.21)	1.00 (0.83, 1.22)	1.02 (0.83, 1.25)
	Middle	1.12 (0.89, 1.41)	0.98 (0.81, 1.17)	0.93 (0.75, 1.14)	1.06 (0.86, 1.30)
	Low	0.96 (0.77, 1.18)	1.04 (0.89, 1.21)	1.04 (0.87, 1.25)	1.02 (0.85, 1.21)
MiBP	High	0.92 (0.64, 1.33)	0.91 (0.70, 1.18)	0.87 (0.63, 1.19)	0.97 (0.74, 1.27)
	Middle	1.23 (0.83, 1.82)	1.07 (0.78, 1.47)	1.14 (0.81, 1.61)	1.07 (0.75, 1.53)
	Low	1.04 (0.76, 1.43)	1.09 (0.85, 1.40)	0.95 (0.72, 1.25)	0.94 (0.68, 1.30)
MnBP	High	1.15 (0.84, 1.57)	0.90 (0.72, 1.14)	1.01 (0.78, 1.32)	0.89 (0.69, 1.15)
	Middle	0.97 (0.71, 1.32)	0.96 (0.76, 1.21)	0.94 (0.72, 1.23)	1.03 (0.76, 1.39)
	Low	0.95 (0.76, 1.19)	0.95 (0.79, 1.14)	0.91 (0.74, 1.13)	0.95 (0.75, 1.20)
MBzP	High	1.10 (0.80, 1.52)	1.01 (0.81, 1.25)	1.17 (0.91, 1.51)	0.97 (0.77, 1.23)
	Middle	0.92 (0.65, 1.30)	1.09 (0.84, 1.40)	1.12 (0.85, 1.48)	0.93 (0.68, 1.26)
	Low	1.09 (0.82, 1.44)	1.05 (0.83, 1.32)	1.06 (0.82, 1.39)	1.09 (0.83, 1.42)
MEHP	High	1.10 (0.78, 1.57)	1.04 (0.83, 1.29)	1.07 (0.84, 1.36)	0.93 (0.72, 1.22)
	Middle	0.99 (0.70, 1.40)	0.94 (0.73, 1.20)	1.02 (0.74, 1.40)	1.04 (0.77, 1.40)
	Low	1.19 (0.88, 1.60)	1.23 (0.97, 1.56)	1.20 (0.91, 1.57)	1.30 (1.01, 1.67)
MEHHP	High	1.17 (0.84, 1.63)	1.06 (0.85, 1.33)	1.01 (0.78, 1.31)	0.97 (0.75, 1.25)
	Middle	1.10 (0.76, 1.58)	1.00 (0.77, 1.30)	1.03 (0.73, 1.46)	0.95 (0.68, 1.32)
	Low	1.19 (0.88, 1.61)	1.36 (1.03, 1.80)	1.24 (0.92, 1.67)	1.35 (1.01, 1.80)
MEOHP	High	1.17 (0.84, 1.63)	1.06 (0.85, 1.33)	1.00 (0.78, 1.29)	0.92 (0.71, 1.19)
	Middle	1.06 (0.73, 1.54)	0.98 (0.75, 1.28)	1.01 (0.72, 1.43)	0.95 (0.68, 1.33)
	Low	1.24 (0.91, 1.68)	1.37 (1.03, 1.81)	1.28 (0.95, 1.72)	1.35 (1.02, 1.80)
MECPP	High	1.12 (0.79, 1.60)	0.99 (0.77, 1.27)	0.90 (0.68, 1.20)	0.91 (0.69, 1.22)
	Middle	0.98 (0.64, 1.51)	0.96 (0.71, 1.30)	1.00 (0.68, 1.45)	0.97 (0.66, 1.41)
	Low	1.15 (0.80, 1.66)	1.29 (0.94, 1.78)	1.17 (0.82, 1.66)	1.27 (0.93, 1.73)
MEPA	High	0.96 (0.82, 1.13)	0.96 (0.86, 1.08)	0.92 (0.81, 1.04)	0.92 (0.80, 1.05)
	Middle	0.99 (0.84, 1.15)	1.04 (0.92, 1.17)	0.96 (0.83, 1.11)	0.99 (0.84, 1.16)
	Low	1.01 (0.88, 1.16)	1.01 (0.91, 1.13)	1.10 (0.98, 1.23)	1.02 (0.90, 1.16)
ETPA	High	0.99 (0.84, 1.16)	0.96 (0.86, 1.08)	0.97 (0.86, 1.09)	1.00 (0.87, 1.14)
	Middle	0.99 (0.86, 1.15)	0.98 (0.88, 1.09)	0.99 (0.87, 1.13)	1.02 (0.88, 1.18)
	Low	1.01 (0.90, 1.12)	1.00 (0.91, 1.09)	1.07 (0.96, 1.20)	1.06 (0.95, 1.18)
PRPA	High	0.98 (0.85, 1.13)	0.98 (0.89, 1.09)	0.95 (0.85, 1.05)	0.96 (0.86, 1.08)
	Middle	0.98 (0.85, 1.14)	1.02 (0.91, 1.14)	0.99 (0.87, 1.13)	1.00 (0.86, 1.16)
	Low	1.04 (0.93, 1.16)	1.04 (0.95, 1.14)	1.10 (0.99, 1.23)	1.02 (0.92, 1.14)

BPA	High	0.98 (0.83, 1.15)	1.06 (0.95, 1.19)	1.06 (0.92, 1.21)	1.01 (0.87, 1.18)
	Middle	0.99 (0.81, 1.21)	1.01 (0.88, 1.17)	1.04 (0.87, 1.25)	0.93 (0.77, 1.13)
	Low	1.06 (0.90, 1.25)	1.02 (0.89, 1.16)	0.96 (0.82, 1.12)	1.06 (0.89, 1.26)
BUPA	High	0.98 (0.84, 1.13)	1.00 (0.90, 1.11)	1.00 (0.90, 1.12)	0.95 (0.85, 1.06)
	Middle	0.98 (0.87, 1.11)	1.00 (0.91, 1.10)	0.98 (0.87, 1.10)	1.02 (0.90, 1.16)
	Low	0.99 (0.90, 1.09)	1.01 (0.93, 1.09)	1.06 (0.97, 1.16)	1.00 (0.91, 1.10)
BP-3	High	1.02 (0.90, 1.16)	0.99 (0.90, 1.08)	1.00 (0.90, 1.10)	1.03 (0.94, 1.14)
	Middle	0.94 (0.83, 1.05)	1.00 (0.92, 1.08)	0.99 (0.88, 1.11)	1.03 (0.93, 1.15)
	Low	1.04 (0.93, 1.16)	1.03 (0.93, 1.12)	1.05 (0.96, 1.16)	1.08 (0.98, 1.20)
TRCS ^a	High	1.16 (0.96, 1.41)	1.05 (0.92, 1.18)	1.03 (0.90, 1.18)	1.03 (0.90, 1.16)
	Middle	0.96 (0.83, 1.12)	1.02 (0.90, 1.15)	1.00 (0.86, 1.17)	1.06 (0.89, 1.26)
	Low	1.00 (0.88, 1.12)	1.01 (0.92, 1.11)	0.94 (0.85, 1.05)	0.98 (0.88, 1.10)
HCB	High	1.26 (0.91, 1.74)	1.06 (0.87, 1.30)	1.15 (0.90, 1.45)	1.22 (0.97, 1.53)
	Middle	1.52 (1.08, 2.15)	1.21 (0.98, 1.51)	1.53 (1.13, 2.07)	1.13 (0.88, 1.44)
	Low	1.00 (0.82, 1.22)	0.99 (0.85, 1.15)	1.18 (0.97, 1.43)	0.93 (0.78, 1.12)
DDE	High	0.95 (0.70, 1.29)	1.08 (0.88, 1.33)	1.39 (1.07, 1.80)	1.16 (0.92, 1.47)
	Middle	1.11 (0.82, 1.49)	0.92 (0.73, 1.16)	1.11 (0.85, 1.44)	0.84 (0.63, 1.12)
	Low	1.23 (1.03, 1.48)	1.00 (0.85, 1.17)	1.13 (0.94, 1.35)	1.01 (0.85, 1.20)
PFHxS	High	0.84 (0.53, 1.35)	0.94 (0.67, 1.31)	1.17 (0.80, 1.70)	0.96 (0.67, 1.38)
	Middle	0.78 (0.45, 1.37)	0.85 (0.59, 1.23)	0.95 (0.61, 1.49)	0.98 (0.60, 1.62)
	Low	0.71 (0.50, 1.01)	0.93 (0.70, 1.23)	1.28 (0.93, 1.76)	1.17 (0.84, 1.63)
PFOA	High	1.27 (0.75, 2.14)	1.03 (0.72, 1.47)	1.14 (0.73, 1.78)	1.07 (0.74, 1.54)
	Middle	0.99 (0.58, 1.69)	1.12 (0.77, 1.63)	1.12 (0.69, 1.83)	0.90 (0.53, 1.51)
	Low	0.90 (0.59, 1.36)	0.98 (0.72, 1.33)	1.21 (0.87, 1.69)	1.15 (0.81, 1.62)
PFOS	High	1.03 (0.58, 1.81)	1.25 (0.87, 1.79)	1.31 (0.82, 2.07)	0.97 (0.65, 1.45)
	Middle	0.91 (0.53, 1.57)	1.01 (0.67, 1.53)	0.99 (0.60, 1.61)	0.92 (0.55, 1.56)
	Low	0.86 (0.57, 1.30)	0.92 (0.66, 1.28)	1.37 (0.95, 1.98)	1.16 (0.80, 1.66)
PFNA	High	0.91 (0.57, 1.46)	1.12 (0.79, 1.59)	1.13 (0.72, 1.78)	1.00 (0.71, 1.41)
	Middle	0.95 (0.58, 1.55)	1.04 (0.70, 1.54)	1.35 (0.84, 2.17)	0.94 (0.57, 1.55)
	Low	1.10 (0.72, 1.69)	1.18 (0.87, 1.60)	1.49 (1.07, 2.07)	1.26 (0.89, 1.79)
PCB 138	High	1.18 (0.81, 1.71)	1.12 (0.88, 1.42)	1.39 (1.02, 1.89)	1.17 (0.89, 1.54)
	Middle	1.20 (0.82, 1.74)	1.06 (0.80, 1.41)	1.15 (0.81, 1.64)	1.00 (0.72, 1.39)
	Low	0.94 (0.73, 1.20)	1.01 (0.83, 1.23)	1.18 (0.93, 1.51)	1.04 (0.82, 1.31)
PCB 153	High	1.22 (0.78, 1.89)	1.07 (0.82, 1.40)	1.48 (1.02, 2.14)	1.00 (0.77, 1.30)
	Middle	1.27 (0.82, 1.98)	0.99 (0.75, 1.33)	1.09 (0.77, 1.56)	0.98 (0.70, 1.37)
	Low	0.87 (0.70, 1.09)	0.95 (0.80, 1.13)	1.21 (0.94, 1.55)	1.05 (0.84, 1.31)
PCB 180	High	1.33 (0.84, 2.10)	1.11 (0.84, 1.46)	1.35 (0.95, 1.92)	0.98 (0.75, 1.29)
	Middle	1.19 (0.75, 1.88)	1.02 (0.77, 1.37)	1.10 (0.75, 1.61)	1.16 (0.79, 1.70)
	Low	0.83 (0.65, 1.05)	1.00 (0.83, 1.22)	1.15 (0.90, 1.48)	1.11 (0.87, 1.41)
Reference outcome category is Class 4: average birth size and subsequent slower BMI gain (High: N = 34.6% / Middle: N = 27% / Low: 38.4%)					
Using imputed data (m=20)					
Abbreviations: BMI = body mass index, RRR = relative risk ratio, CI = confidence interval					

^a TRCS only included two cohorts (Sabadell, Valencia) as such sample size was smaller (n = 375 for High, n = 374 for middle, n = 606 for lower).

All models adjusted for sub-cohort, smoking during pregnancy, parity, maternal age at delivery, maternal prepregnancy BMI, paternal prepregnancy BMI, maternal Mediterranean diet score, child sex.

Bold text indicates significant result.

Table S10. Associations between EDC mixture and childhood BMI trajectories from mixture models using BWQS regression (n = 1,911), for the INMA birth cohort study.

	Class 1 Higher birth size – accelerated BMI gain			Class 2 Higher birth size – slower BMI gain			Class 3 Lower birth size – slower BMI gain			Class 5 Lower birth size – slower BMI gain		
	OR	lower CrI	upper CrI	OR	lower CrI	upper CrI	OR	lower CrI	upper CrI	OR	lower CrI	upper CrI
OR (BWQS index)	1.15	0.68	1.97	1.16	0.86	1.59	1.71	1.03	2.60	1.24	0.82	1.87
Chemical weight for:												
MEP	0.048	0.001	0.169	0.044	0.001	0.152	0.030	0.001	0.106	0.051	0.001	0.182
MiBP	0.039	0.001	0.136	0.041	0.001	0.144	0.022	0.001	0.084	0.039	0.001	0.140
MnBP	0.046	0.001	0.162	0.042	0.001	0.152	0.028	0.001	0.097	0.039	0.001	0.139
MBzP	0.041	0.001	0.137	0.042	0.001	0.142	0.029	0.001	0.101	0.034	0.001	0.127
MEHP	0.044	0.001	0.151	0.042	0.001	0.154	0.037	0.001	0.128	0.039	0.001	0.146
MEHHP	0.042	0.001	0.157	0.045	0.001	0.154	0.031	0.001	0.112	0.038	0.001	0.141
MEOHP	0.040	0.001	0.146	0.041	0.001	0.147	0.026	0.001	0.101	0.036	0.001	0.128
MECPP	0.039	0.001	0.144	0.040	0.001	0.146	0.029	0.001	0.101	0.039	0.001	0.128
MEPA	0.039	0.001	0.141	0.043	0.001	0.150	0.027	0.001	0.099	0.041	0.001	0.145
ETPA	0.039	0.001	0.155	0.038	0.001	0.135	0.026	0.001	0.092	0.042	0.001	0.152
PRPA	0.041	0.001	0.147	0.048	0.001	0.163	0.032	0.001	0.115	0.044	0.001	0.151
BPA	0.045	0.001	0.163	0.049	0.002	0.170	0.043	0.001	0.140	0.047	0.001	0.163
BUPA	0.040	0.001	0.139	0.039	0.001	0.140	0.029	0.001	0.099	0.039	0.001	0.143
BP-3	0.050	0.001	0.179	0.046	0.001	0.157	0.051	0.002	0.161	0.066	0.002	0.215
HCB	0.059	0.002	0.212	0.052	0.002	0.172	0.108	0.004	0.283	0.044	0.001	0.158
DDE	0.055	0.002	0.197	0.048	0.002	0.168	0.094	0.002	0.261	0.055	0.002	0.187
PFHxS	0.039	0.001	0.156	0.037	0.001	0.137	0.040	0.001	0.132	0.042	0.001	0.143
PFOA	0.040	0.001	0.147	0.039	0.001	0.144	0.034	0.001	0.125	0.042	0.001	0.149
PFOS	0.039	0.001	0.150	0.039	0.001	0.142	0.047	0.001	0.161	0.045	0.001	0.150
PFNA	0.039	0.001	0.139	0.045	0.001	0.158	0.043	0.001	0.134	0.050	0.001	0.177
PCB 138	0.045	0.001	0.156	0.048	0.001	0.171	0.075	0.003	0.235	0.043	0.001	0.148
PCB 153	0.045	0.001	0.157	0.045	0.001	0.158	0.063	0.002	0.197	0.042	0.001	0.146
PCB 180	0.046	0.001	0.165	0.047	0.001	0.168	0.058	0.002	0.192	0.045	0.001	0.157

Reference outcome category is Class 4: average birth size and subsequent slower BMI gain

Abbreviations: BMI = body mass index, OR = odds ratio, CrI = credible interval

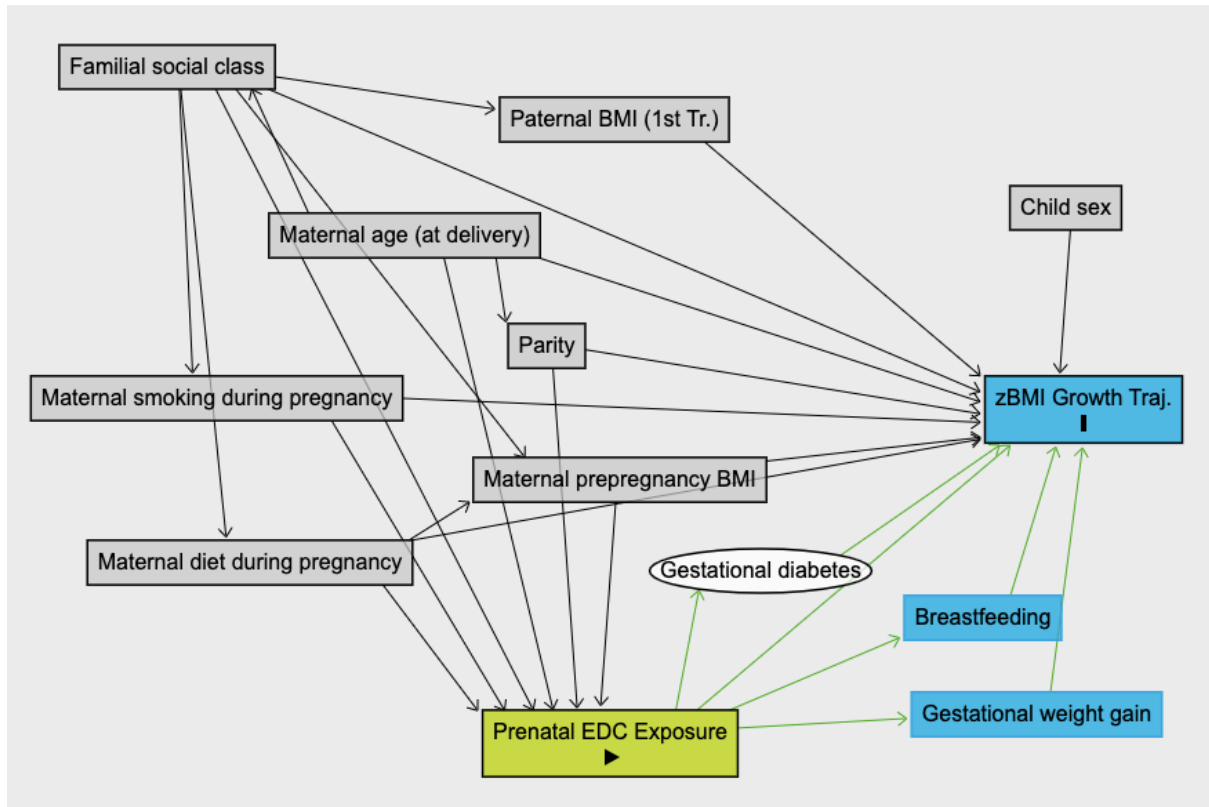
All models adjusted for sub-cohort, smoking during pregnancy, parity, maternal age at delivery, maternal prepregnancy BMI, paternal prepregnancy BMI, maternal Mediterranean diet score, social class, child sex.

Table S11. Class-specific mean predicted trajectory values and their confidence intervals for each BMI trajectory class depicted in Figure 1, by select age groups.

Age	Class 1	Class 2	Class 3	Class 4	Class 5
6 mo.	0.61 (0.56, 0.66)	0.34 (0.30, 0.39)	-0.66 (-0.71, -0.60)	-0.41 (-0.46, -0.36)	-1.31 (-1.36, -1.25)
1 year	1.14 (1.10, 1.18)	0.60 (0.57, 0.64)	-0.19 (-0.24, -0.15)	-0.19 (-0.24, -0.15)	-1.11 (-1.15, -1.07)
2 years	1.57 (1.53, 1.62)	0.80 (0.76, 0.84)	0.22 (0.17, 0.27)	-0.03 (-0.07, 0.02)	-0.94 (-0.99, -0.90)
3 years	2.17 (2.11, 2.23)	1.02 (0.97, 1.08)	0.87 (0.80, 0.93)	0.18 (0.13, 0.23)	-0.71 (-0.77, -0.65)
5 years	2.48 (2.41, 2.54)	1.07 (1.01, 1.13)	1.33 (1.26, 1.39)	0.24 (0.20, 0.29)	-0.57 (-0.63, -0.50)
7 years	2.47 (2.40, 2.55)	0.85 (0.78, 0.92)	1.80 (1.73, 1.87)	0.12 (0.07, 0.17)	-0.49 (-0.56, -0.42)
9 years	2.11 (2.02, 2.21)	0.57 (0.48, 0.65)	1.90 (1.82, 1.98)	-0.07 (-0.13, -0.01)	-0.49 (-0.57, -0.41)

The “class-specific mean predicted trajectory” values are generated by the model function. The values are representative of the mean zbmi predicted at a chosen age point for each trajectory. These values are estimated through simulations, in our case we used 50,000 simulations. Class 1: higher birth size – accelerated BMI gain (N=212, 11.1%). Class 2: higher birth size – slower BMI gain (N=513, 26.8%). Class 3: lower birth size – accelerated BMI gain (N=292, 15.3%). Class 4: average birth size – slower BMI gain (N=607, 31.8%) (reference). Class 5: lower birth size – slower BMI gain (N=287, 15.0%).

Figure S1. Directed acyclic graph of the association between prenatal exposure to EDCs and zBMI growth trajectories.



Abbreviations: BMI, body mass index; EDCs, endocrine disrupting chemicals; Traj., trajectories; Tr., trimester.

Blue nodes: Variables associated to growth trajectories. Grey nodes: variables associated to both exposure and outcomes (confounders), with the exception of child sex. White nodes: variables unaccounted.

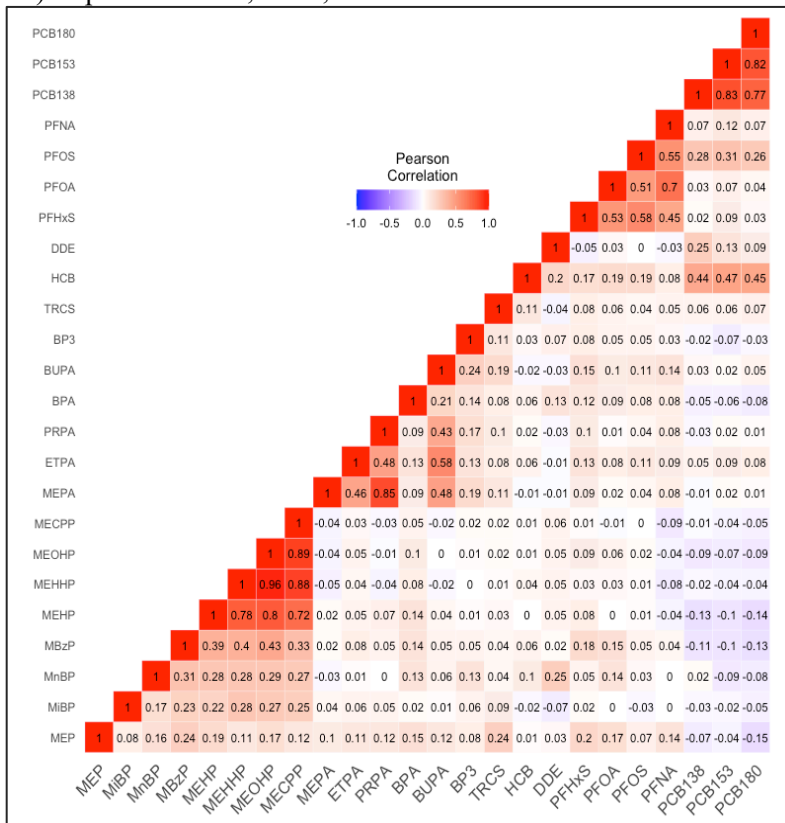
Including only those variables with the grey nodes, the model is considered to be sufficiently adjusted for the estimation of the total effect.

DAG created using Daggity¹

1. Textor J, van der Zander B, Gilthorpe MS, Liškiewicz M, Ellison GT (2016). "Robust causal inference using directed acyclic graphs: the R package 'dagitty'." *International Journal of Epidemiology*, 45(6), 1887–1894. [doi:10.1093/ije/dyw341](https://doi.org/10.1093/ije/dyw341).

Figures S2-3. Pairwise Correlations of EDC exposures for the INMA birth cohort study

S2) Imputed data set, n = 1,911



S3) Unimputed data set, complete case

