Supplemental Material

Prenatal Phthalate Exposure and Childhood Growth and Blood Pressure: Evidence from the Spanish INMA-Sabadell Birth Cohort Study

Damaskini Valvi, Maribel Casas, Dora Romaguera, Nuria Monfort, Rosa Ventura, David Martinez, Jordi Sunyer, and Martine Vrijheid
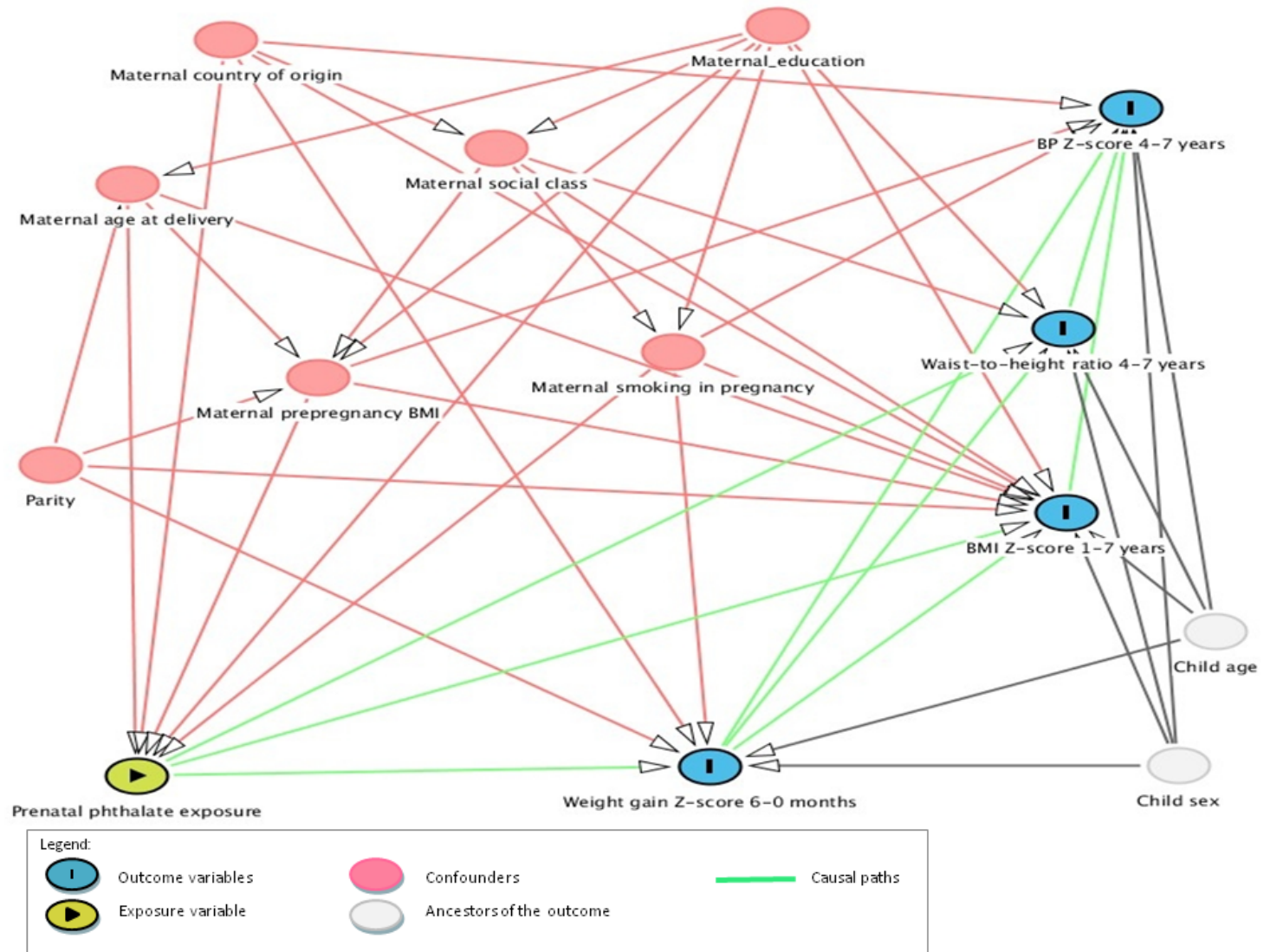
Table of Contents

Figure S1. Directed Acyclic Graph of the known or assumed relationships between covariates retained in the final models.
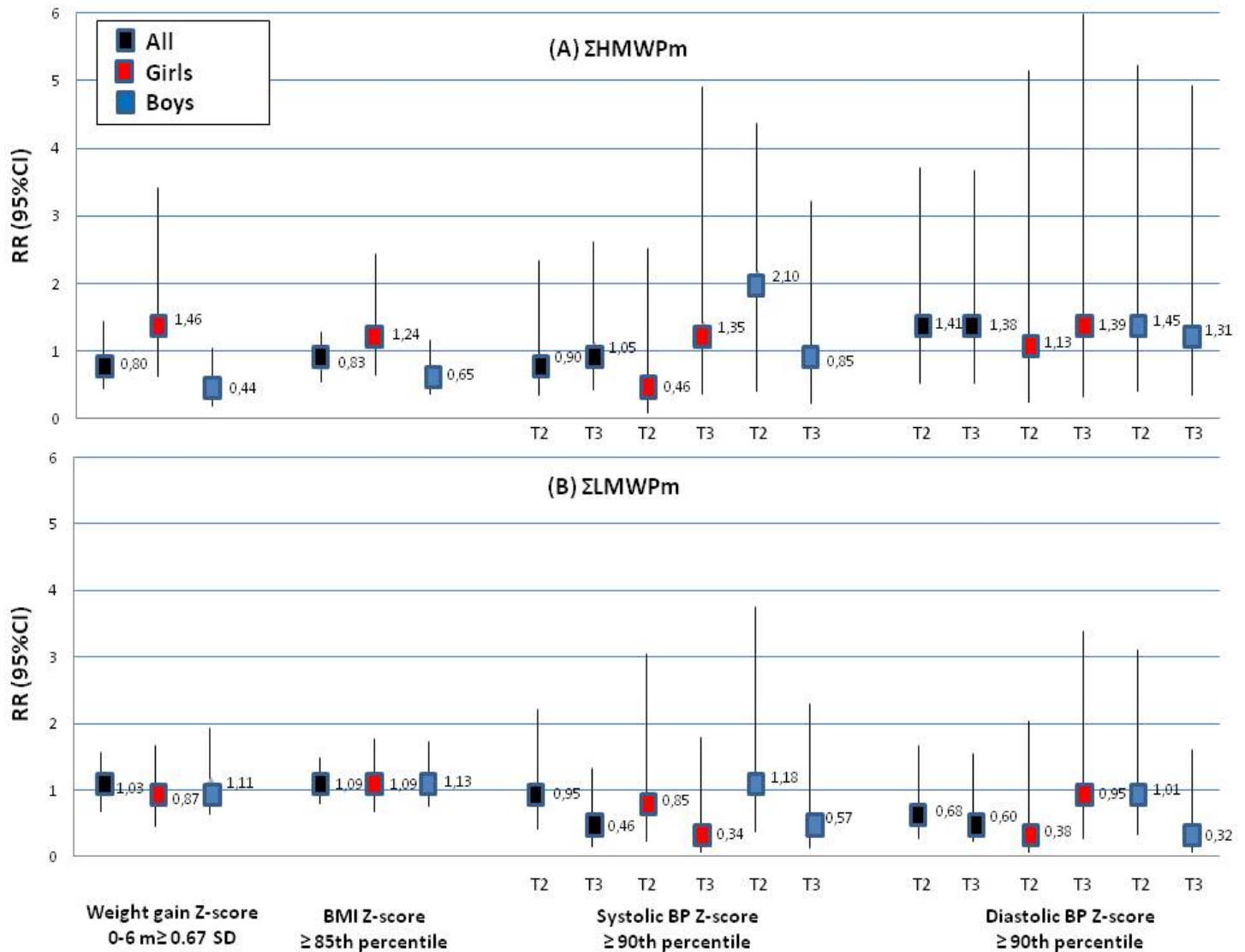
Figure S2. Associations between the average 1st-3rd pregnancy trimester concentrations of ΣHMWPm (A) and ΣLMWPm (B) metabolites (log$_2$-transformed, in μg-g creatinine) and dichotomous outcomes. All models adjusted for child sex, exact age at examination and maternal characteristics (country of origin, age at delivery, parity, education, social class, prepregnancy BMI and smoking in pregnancy). Effect estimates for systolic and diastolic BP are shown per tertile of exposure (i.e. T2: tertile 2; T3: tertile 3). The RR in the reference groups is 1. (Phthalate exposure modeled continuously for all other outcomes).

3

Table S1. Average 1st-3rd pregnancy trimester concentrations of ΣDEHPm and MBzP metabolites ($\log_2$-transformed, in µg-g creatinine) and growth and BP outcomes.

Outcome/Age at examination		ΣDEHPm[a]			MBzP[a]		
		Girls β (95% CI)	Boys β (95% CI)	P-sex interaction	Girls β (95% CI)	Boys β (95% CI)	P-sex interaction
Weight gain Z-score 0-6 months		n=186	n=205		n=186	n=205	
		0.26 (-0.13, 0.65)	-0.36 (-0.70, -0.01)	0.01	0.02 (-0.28, 0.31)	-0.28 (-0.55, -0.01)	0.09
BMI Z-score[b]		n=186/525	n=205/582		n=186/525	n=205/582	
All ages		0.21 (-0.11, 0.53)	-0.32 (-0.64, -0.02)	0.03	0.10 (-0.16, 0.38)	-0.16 (-0.33, 0.15)	0.76
Systolic BP Z-score[b,c]		n=181/339	n=198/358		n=181/339	n=198/358	
All ages	T2	-0.50 (-0.77, -0.24)	-0.01 (-0.24, 0.21)	0.01	-0.05 (-0.29, 0.25)	-0.10 (-0.34, 0.13)	0.41
	T3	-0.37 (-0.63, -0.10)	-0.05 (-0.29, 0.18)	0.10	-0.16 (-0.40, 0.10)	-0.15 (-0.37, 0.07)	0.45
Diastolic BP Z-score[b,c]		n=181/339	n=198/358		n=181/339	n=198/358	
All ages	T2	-0.10 (-0.34, 0.15)	0.13 (-0.10, 0.34)	0.44	0.03 (-0.19, 0.29)	-0.02 (-0.36, 0.26)	0.62
	T3	-0.08 (-0.33, 0.17)	0.05 (-0.17, 0.27)	0.93	-0.05 (-0.17, 0.27)	0.16 (-0.15, 0.47)	0.45

All models adjusted for child sex, exact age at examination and maternal characteristics (country of origin, age at delivery, parity, education, social class, prepregnancy BMI and smoking in pregnancy).

[a]Pearson correlation coefficients ranged from 0.68 to 0.97 for pairs of metabolites included in ΣDEHPm and from 0.17 to 0.32 for pairs of DEHP metabolites and MBzP. [b]Coefficients estimated by GEE models. N represents numbers of individuals/outcome measures. [c]Effect estimates shown per tertile of exposure (i.e. T2: tertile 2; T3: tertile 3). The *β* in the reference groups is 0.

Table S2. Average 1st-3rd pregnancy trimester concentrations of MEP, MiBP and MnBP metabolites ($\log_2$-transformed, in μg-g creatinine) and BP outcomes.

Outcome/Age at examination		MEP[a]		MiBP[a]		MnBP[a]	
		Girls β (95% CI)	Boys β (95% CI)	Girls β (95% CI)	Boys β (95% CI)	Girls β (95% CI)	Boys β (95% CI)
Weight gain Z-score 0-6 months		n=186	n=205	n=186	n=205	n=186	n=205
		-0.05 (-0.29, 0.18)	0.09 (-0.15, 0.34)	0.09 (-0.27, 0.46)	-0.18 (-0.53, 0.15)	-0.14 (-0.42, 0.13)	-0.13 (-0.46, 0.21)
BMI Z-score[b]		n=186/525	n=205/582	n=186/525	n=205/582	n=186/525	n=205/582
All ages		0.08 (-0.16, 0.31)	0.01 (-0.24, 0.26)	-0.01 (-0.38, 0.35)	-0.11 (-0.47, 0.26)	-0.11 (-0.39, 0.18)	0.03 (-0.31, 0.38)
Systolic BP Z-score[b,c]		n=181/339	n=198/358	n=181/339	n=198/358	n=181/339	n=198/358
All ages	T2	-0.15 (-0.41, 0.12)	0.04 (-0.19, 0.28)	-0.10 (-0.45, 0.15)	0.08 (-0.17, 0.31)	-0.12 (-0.40, 0.16)	0.02 (-0.22, 0.26)
	T3	-0.44 (-0.71, -0.18)**	0.20 (-0.06, 0.44)**	-0.11 (-0.51, 0.11)	0.07 (-0.27, 0.21)	-0.08 (-0.42, 0.23)	-0.01 (-0.27, 0.21)
Diastolic BP Z-score[b,c]		n=181/339	n=198/358	n=181/339	n=198/358	n=181/339	n=198/358
All ages	T2	-0.17 (-0.42, 0.08)	-0.01 (-0.23, 0.22)	-0.06 (-0.30, 0.29)	0.20 (-0.07, 0.40)	-0.10(-0.36, 0.10)	-0.06 (-0.19 0.20)
	T3	-0.23 (-0.48, 0.04)	-0.07 (-0.30, 0.16)	0.03 (-0.19, 0.30)	0.12 (-0.12, 0.35)	-0.05 (-0.22, 0.20)	-0.00 (-0.26, 0.20)

All models adjusted for child sex, exact age at examination and maternal characteristics (country of origin, age at delivery, parity, education, social class, prepregnancy BMI and smoking in pregnancy).

[a]Pearson correlation coefficients: 0.12 for MEP-MiBP, 0.15 for MEP-MnBP and 0.46 for MiBP-MnBP. [b]Coefficients estimated by GEE models. N represents numbers of individuals/outcome measures. [c]Effect estimates shown per tertile of exposure (i.e. T2: tertile 2; T3: tertile 3). The β in the reference groups is 0. P-value for the interaction term between exposure and child age at examination >0.25 for all models shown in this table.

P-sex interaction: **<0.05.