**Supplemental Material**

First trimester maternal exposures to endocrine disrupting chemicals and metals and fetal size in the Michigan Mother Infant Pairs study

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Table S1. Sex-Stratified Anthropometric Measures

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Females (n=29)** | | **Males (n=27)** | |
|  | *Median* | *Range* | *Median* | *Range* |
| Birthweight (g) | 3410 | (2805 - 4070) | 3640 | (2860 - 4685) |
| Fenton z-score % tile | 54.4 | (6.6 - 85.2) | 62.7 | (12.8 - 95.1) |
| Fetal Anthropometry a |  |  |  |  |
| Abdominal circ. | 137 | (111 – 161) | 140 | (127 – 242) |
| Biparietal diameter | 43.4 | (36 – 48) | 44 | (40 – 70.4) |
| Femur length | 29.6 | (23 – 36) | 29.4 | (24 – 51.4) |
| Head circ.b | 161 | (135 – 182) | 164 | (155 – 265) |

a Units= mm; b Circ: circumference

Table S2. Correlations of phthalate metabolites in first trimester maternal urine samples (n=56)

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Phthalate | MnBP | MBzP | mCINP | MCOMHP | MCPP | MeCPP | MEHHP | MEHP | MEOHP | MEP | MiBP |
| MnBP |  | **0.79** | **0.65** | **0.79** | **0.68** | **0.78** | **0.77** | **0.74** | **0.79** | **0.54** | **0.81** |
| MBzP | <0.001 |  | **0.59** | **1.00** | **0.58** | **0.73** | **0.72** | **0.70** | **0.71** | **0.29** | **0.72** |
| mCINP | <0.001 | <0.001 |  | **0.59** | **0.88** | **0.77** | **0.66** | **0.69** | **0.67** | **0.32** | **0.60** |
| MCOMHP | <0.001 | <0.001 | <0.001 |  | **0.58** | **0.73** | **0.72** | **0.70** | **0.71** | **0.29** | **0.71** |
| MCPP | <0.001 | <0.001 | <0.001 | <0.001 |  | **0.76** | **0.66** | **0.67** | **0.68** | **0.38** | **0.60** |
| MeCPP | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |  | **0.92** | **0.85** | **0.92** | **0.40** | **0.76** |
| MEHHP | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |  | **0.91** | **0.99** | **0.45** | **0.75** |
| MEHP | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |  | **0.91** | **0.34** | **0.68** |
| MEOHP | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |  | **0.48** | **0.76** |
| MEP | <0.001 | 0.03 | 0.02 | 0.03 | 0.004 | 0.002 | 0.001 | 0.01 | <0.001 |  | **0.48** |
| MiBP | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | 0.001 |  |

Above diagonal denotes spearman correlation; Below diagonal denotes p-value associated with correlation value

Table S3. Correlations of phenols in first trimester maternal urine samples (n=56)

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Phenol | 2,4-DCP | 2,5-DCP | BP-3 | BPA | BPF | BPS | BuPB | EtPb | MePB | PrPB | TCS |
| 2,4-DCP |  | **0.64** | **0.43** | **0.65** | **0.30** | **0.5** | 0.04 | **0.50** | **0.46** | 0.19 | **0.60** |
| 2,5-DCP | <0.001 |  | **0.29** | **0.55** | 0.20 | **0.33** | 0.04 | **0.31** | **0.31** | 0.04 | **0.44** |
| BP-3 | 0.001 | 0.03 |  | **0.30** | **0.30** | **0.26** | 0.06 | **0.44** | **0.43** | **0.33** | **0.44** |
| BPA | <0.001 | <0.001 | 0.02 |  | **0.31** | **0.46** | 0.08 | **0.41** | **0.36** | 0.13 | 0.40 |
| BPF | 0.03 | 0.14 | 0.03 | 0.02 |  | 0.12 | -0.06 | **0.40** | 0.19 | 0.24 | 0.19 |
| BPS | <0.001 | 0.01 | 0.05 | <0.001 | 0.39 |  | 0.11 | 0.17 | **0.51** | **0.35** | **0.32** |
| BuPB | 0.79 | 0.75 | 0.67 | 0.55 | 0.64 | 0.41 |  | 0.15 | 0.05 | 0.07 | -0.09 |
| EtPB | <0.001 | 0.02 | 0.001 | 0.002 | 0.003 | 0.22 | 0.28 |  | **0.44** | **0.44** | **0.37** |
| MePB | 0.003 | 0.02 | 0.001 | 0.01 | 0.15 | <0.001 | 0.72 | 0.001 |  | 0.81 | 0.45 |
| PrPB | 0.16 | 0.79 | 0.01 | 0.32 | 0.08 | 0.01 | 0.59 | 0.001 | <0.001 |  | 0.21 |
| TCS | <0.001 | 0.001 | 0.001 | 0.002 | 0.15 | 0.02 | 0.53 | 0.01 | 0.001 | 0.12 |  |

Above diagonal denotes spearman correlation; Below diagonal denotes p-value associated with correlation value

Table S4. Correlations of metals in first trimester maternal urine samples (n=55)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Metal | As | Ba | Cd | Cr | Cu | Hg | Mn | Mo | Ni | Pb | Se | Sn | Tl | Zn |
| As |  | **0.35** | **0.58** | **0.50** | **0.56** | **0.31** | **0.57** | **0.67** | **0.69** | **0.45** | **0.78** | **0.62** | **0.55** | **0.70** |
| Ba | 0.01 |  | **0.39** | **0.54** | 0.15 | -0.10 | 0.13 | 0.20 | **0.28** | **0.29** | **0.30** | **0.36** | **0.28** | 0.15 |
| Cd | <0.001 | 0.02 |  | **0.64** | **0.65** | 0.18 | **0.66** | **0.66** | **0.74** | **0.54** | **0.73** | **0.66** | **0.53** | **0.66** |
| Cr | <0.001 | <0.001 | <0.001 |  | 0.55 | -0.09 | **0.54** | **0.54** | **0.58** | **0.42** | **0.59** | **0.50** | **0.45** | **0.52** |
| Cu | <0.001 | 0.28 | <0.001 | <0.001 |  | 0.24 | **0.72** | **0.60** | **0.80** | **0.64** | **0.71** | **0.69** | **0.47** | **0.72** |
| Hg | 0.02 | 0.45 | 0.19 | 0.51 | 0.07 |  | 0.22 | **0.29** | 0.24 | 0.20 | 0.21 | 0.24 | 0.19 | **0.30** |
| Mn | <0.001 | 0.35 | <0.001 | <0.001 | <0.001 | 0.11 |  | **0.60** | **0.75** | **0.53** | **0.76** | **0.71** | **0.52** | **0.66** |
| Mo | <0.001 | 0.15 | <0.001 | <0.001 | <0.001 | 0.03 | <0.001 |  | **0.72** | **0.37** | **0.74** | **0.66** | **0.42** | **0.68** |
| Ni | <0.001 | 0.04 | <0.001 | <0.001 | <0.001 | 0.08 | <0.001 | <0.001 |  | **0.69** | **0.80** | **0.71** | **0.52** | **0.78** |
| Pb | 0.001 | 0.03 | <0.001 | 0.001 | <0.001 | 0.15 | <0.001 | 0.01 | <0.001 |  | **0.46** | **0.59** | **0.47** | **0.56** |
| Se | <0.001 | 0.02 | <0.001 | <0.001 | <0.001 | 0.13 | <0.001 | <0.001 | <0.001 | 0.001 |  | **0.75** | **0.51** | **0.85** |
| Sn | <0.001 | 0.01 | <0.001 | <0.001 | <0.001 | 0.08 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |  | **0.56** | **0.67** |
| Tl | <0.001 | 0.04 | <0.001 | 0.001 | <0.001 | 0.17 | <0.001 | 0.001 | <0.001 | 0.003 | <0.001 | <0.001 |  | **0.48** |
| Zn | <0.001 | 0.27 | <0.001 | <0.001 | <0.001 | 0.03 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |  |

Above diagonal denotes spearman correlation; Below diagonal denotes p-value associated with correlation value

Table S5. Distribution of summed chemicals among MMIP women (n=56)

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| ∑ score | N a | Mean | SD | Min | P10 | P25 | P50 | P75 | P95 | P99 | Max |
| Phthalates | 12 | 12.18 | 7.38 | 1 | 1 | 6 | 11 | 19 | 23 | 23 | 23 |
| Phenols | 12 | 12.45 | 5.31 | 3 | 6 | 8 | 12 | 17 | 22 | 22 | 22 |
| Metals b | 17 | 17.15 | 8.58 | 3 | 6 | 10 | 18 | 25 | 30 | 32 | 32 |
| Total b | 41 | 41.46 | 19.71 | 7 | 16 | 24 | 39.5 | 62 | 71 | 75 | 75 |

a N=number of chemicals/elements measured; b n=55 women

Concentration ranks assigned were 0, 1, and 2; Maximum possible score for phthalates and metals = 24, metals = 34, and total = 82

Table S6. Bivariate associations of phthalate metabolites and survey responses among MMIP women

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Metabolite | | | | | | | | | | | | | | | | | | | | | |
|  | MnBP | | MBzP | | MCOMHP | | mCINP | | MCPP | | meCPP | | MEHHP | | MEHP | | MEOHP | | MEP | | MiBP | |
|  | M | p | M | p | M | p | M | p | M | p | M | p | M | p | M | p | M | p | M | p | M | p |
| P&Ca No Yes | 1.55 2.04 | 0.14 | 7.52 15.99 | 0.76 | 7.51 15.99 | 0.75 | 2.70 1.90 | 0.90 | 4.07 4.55 | 0.50 | 8.94 8.87 | 0.50 | 8.27 9.33 | 0.26 | 2.01 3.18 | 0.23 | 3.92 5.20 | 0.18 | 22.46 83.71 | 0.10 | 6.45 6.09 | 0.36 |
| Haira No  Yes | 11.22 11.60 | 0.42 | 13.10 14.31 | 0.06 | 13.10 14.30 | 0.06 | 2.18 2.07 | 0.31 | 6.66 3.77 | 0.09 | 10.99  8.24 | 0.12 | 12.25 8.12 | 0.08 | 3.96 2.58 | 0.08 | 7.15 4.22 | 0.08 | 166.74 40.09 | 0.42 | 7.97  5.63 | 0.23 |
| FFb  No  Yes | 17.51 8.19 | **0.004** | 15.90 10.66 | 0.10 | 15.90 10.66 | 0.10 | 1.44 3.24 | **0.002** | 2.51 7.91 | **0.04** | 6.15 13.81 | **0.02** | 7.49 11.95 | 0.20 | 2.50 3.63 | 0.17 | 3.80 6.68 | 0.14 | 79.30 51.84 | 0.17 | 4.24 9.65 | **0.01** |

a no (n=13) yes (n=43); b no (n=36) yes (n=20)

M: Median; p: p-value; P&C: Perfume and Cosmetics; Hair: Haircare Products; FF: Fast Food; FV: Fresh Vegetables

Table S7. Bivariate associations for phenols and survey responses among MMIP women

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Phenols | | | | | | | | | | | | | |
|  | 2,4-DCP | | 2,5-DCP | | BP-3 | | BPA | | | BPF | | | BPS | |
|  | M | P | M | P | M | P | M | P | M | | P | M | | P |
| Perfume & Cosmetic  No  Yes | 0.23 0.33 | 0.31 | 0.20 0.29 | 0.30 | 58.22 49.64 | 0.80 | 0.72 0.83 | 0.63 | 0.14 0.14 | | 0.84 | 0.14 0.14 | | 0.06 |
| Hair products  No  Yes | 0.24 0.74 | 0.57 | 0.22 0.61 | 0.35 | 51.24 47.12 | **0.01** | 0.70 1.06 | 0.34 | 0.14 0.14 | | 0.75 | 0.14 0.14 | | 0.82 |
| Canned Food  No  Yes | 0.25 0.34 | 0.66 | 0.22 0.31 | 0.50 | 39.52 58.22 | 0.60 | 0.83 0.64 | 0.57 | 0.14 0.14 | | **0.03** | 0.14 0.14 | | 0.76 |
| Fast food  No  Yes | 0.24 0.74 | 0.11 | 0.22 0.61 | **0.03** | 51.24 47.12 | 0.75 | 0.70 1.06 | 0.40 | 0.14 0.14 | | 0.50 | 0.14 0.14 | | 0.37 |
|  |  |  |  |  |  |  |  |  |  | |  |  | |  |
|  |  |  |  |  |  |  |  |  |  | |  |  | |  |

Note: Equivalent medians may result from low detection rates

Table S7 cont’d. Bivariate associations for phenols and survey responses among MMIP women

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Phenols | | | | | | | | | | |
|  | BuPB | | EtPb | | MePB | | PrPB | | TCS | | |
|  | M | P | M | P | M | P | M | P | | M | P |
| Perfume & Cosmetic  No  Yes | 0.14 0.14 | 0.28 | 0.73 0.42 | 0.69 | 15.55 93.60 | 0.06 | 6.88 15.32 | 0.24 | | 13.20 17.05 | 0.64 |
| Hair products  No  Yes | 0.14 0.14 | 0.64 | 0.28 2.31 | 0.86 | 25.27 98.38 | 0.21 | 7.51 22.16 | 0.35 | | 11.18 28.95 | 0.21 |
| Canned Food  No  Yes | 0.14 0.14 | 0.72 | 1.00 0.48 | 0.66 | 75.87 53.06 | 0.71 | 7.96 15.32 | 0.81 | | 15.47 13.74 | 0.87 |
| Fast food  No  Yes | 0.14 0.14 | 0.57 | 0.28 2.31 | 0.08 | 25.27 98.38 | **0.03** | 7.51 22.16 | 0.08 | | 11.18 28.95 | **0.03** |

Table S8. Bivariate associations with bisphenol A, F, and S and canned food consumption (n=56)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | | | | Bisphenol | |  | |
|  | BPA | | | | BPF | | BPS | |
|  | M | p-value | M | p-value | | M | | p-value |
| Canned food consumption  No  Yes | 0.83 0.64 | 0.57 | 0.14 0.14 | **0.03** | | 0.14 0.14 | | 0.76 |
| Canned food frequency  None  ≤ 1 serving/day  2-3 servings/day  ≥ 4 servings/day | 1.20 1.34  4.58 - | 0.21 | 0.32 1.39 6.52 - | **0.02** | | 0.25 0.32  0.26 - | | 0.58 |

M: Median

Table S9. Bivariate associations for metals and survey responses among MMIP women

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Metals | | | | | | | | | | | | | | | | | |
|  | As | | Ba | | Cd | | | Cr | | | Cu | | Hg | | | Mn | | |
|  | M | P | M | P | M | P | M | | P | M | | P | | M | P | | M | P | |
| Perfume & Cosmetic  No  Yes | 2.75 4.26 | 0.26 | 5.96 4.60 | 0.82 | 0.04 0.06 | 0.14 | 0.59  0.72 | | 0.37 | 7.76 9.36 | | 0.93 | | 0.09 0.04 | 0.33 | | 1.24 1.67 | 0.27 | |
| Hair products  No  Yes | 4.57 3.68 | 0.46 | 2.95 4.91 | 0.39 | 0.07 0.04 | 0.49 | 0.71 0.71 | | 0.75 | 9.69 9.13 | | 0.49 | | 0.07 0.06 | 0.70 | | 1.97 1.40 | 0.09 | |
| Canned Food  No  Yes | 3.66 4.47 | 0.21 | 4.60 4.73 | 0.48 | 0.04 0.51 | 0.41 | 0.69 0.72 | | 0.57 | 7.66 10.40 | | 0.79 | | 0.04 0.08 | 0.08 | | 1.54 1.54 | 0.85 | |
| Fast food  No  Yes | 3.68 4.47 | 0.40 | 4.10 4.82 | 0.28 | 0.04 0.13 | 0.02 | 0.68 0.83 | | 0.34 | 7.33 11.83 | | 0.07 | | 0.04 0.06 | 0.64 | | 1.28 1.74 | 0.15 | |

M: Median; P: P-value

Table S9 cont’d. Bivariate associations for metals and survey responses among MMIP women

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Metals | | | | | | | | | | | | | | | | |
|  | Mo | | Ni | | Pb | | | Se | | | Sn | | | Tl | | Zn | |
|  | M | P | M | P | M | P | M | | P | M | | P | M | | P | M | P |
| Perf. & Cosmetic  No  Yes | 50.13 47.27 | 0.71 | 2.73 4.80 | 0.23 | 0.13 0.25 | 0.21 | 33.82  51.85 | | 0.28 | 0.19 0.38 | | 0.28 | 0.15 0.19 | | 0.28 | 171.04 235.48 | 0.61 |
| Hair products  No  Yes | 68.30 40.47 | 0.13 | 4.94 3.91 | 0.55 | 0.23 0.21 | 0.42 | 52.82 44.51 | | 0.29 | 0.45 0.27 | | 0.58 | 0.20 0.17 | | 0.11 | 200.82 178.03 | 0.52 |
| Canned Food  No  Yes | 41.25 61.00 | 0.06 | 3.91 5.01 | 0.48 | 0.17 0.28 | 0.11 | 42.13 50.98 | | 0.30 | 0.29 0.39 | | 0.09 | 0.15 0.20 | | 0.60 | 169.82 254.41 | 0.32 |
| Fast food  No  Yes | 40.47 81.86 | 0.07 | 3.16 4.92 | 0.06 | 0.17  0.28 | 0.31 | 36.05 66.06 | | **0.01** | 0.18 0.50 | | **0.02** | 0.15 0.19 | | 0.22 | 170.65 332.71 | **0.02** |

M: Median; P: P-value

Table S10. Associations between Bisphenol F and S dichotomized by detected vs. not detected and birth

outcomes (n=56)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | Birth outcomes | | | | | | |
|  | Birth weight (g) a | | |  | Fenton z-score b | | |
| Phenol | β | (95% CI) | p-value |  | Β | (95% CI) | p-value |
| BPF | -7.88 | (-270.32, 254.56) | 0.95 |  | -0.18 | (-0.73, 0.37) | 0.52 |
| BPS | **-220.10** | **(-424.94, -15.26)** | **0.04** |  | **-0.51** | **(-0.94, -0.07)** | **0.02** |

a Adjusted for Specific gravity, gestational age, and gender; b Adjusted for Specific gravity;