**Supplemental Material For:** Associations of parental preconception and prenatal urinary bisphenol A and paraben concentrations with child behavior

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Contents

**Supplemental Table 1**: Comparison of baseline characteristics of the study sample to the original EARTH cohort 2

**Supplemental Table 2:** Distribution of specific gravity standardized preconception urinary phenol concentrations in women and men in the EARTH study 3

**Supplemental Table 3:** Pearson's correlation coefficients between parental urinary

bisphenol A and ∑paraben concentrations 4

**Supplemental Table 4:** Adjusted mean differences in the BASC-2 behavioral symptoms index, internalizing, and externalizing problems T-Scores stratified by child sex with loge-unit increase in maternal and paternal preconception and maternal pregnancy urinary bisphenol A and ∑paraben concentrations 5

**Supplemental Table 5:** Adjusted difference in the BASC-2 behavioral symptoms index, internalizing, and externalizing problems T-Scores among children younger than 6 years old per ln-unit increase in maternal and paternal preconception and maternal prenatal urinary bisphenol A and ∑paraben concentrations 6

**Supplemental Table 6:** Adjusted difference in the BASC-2 behavioral symptoms

index, internalizing, and externalizing problems T-Scores among singleton children with

loge-unit increase in maternal and paternal preconception and maternal pregnancy

urinary bisphenol A and ∑paraben concentrations 7

**Supplemental Table 7:** Adjusted difference in the BASC-2 behavioral symptoms index, internalizing, and externalizing problems T-Scores among children with a gestation > 37 weeks with loge-unit increase in maternal and paternal preconception urinary bisphenol A and ∑paraben concentrations 8

**Supplemental Table 8**: Difference in externalizing problems t-score with loge-unit increase in maternal preconception urinary BPA concentration 9

**Supplemental Table 9**: Adjusted difference in the BASC-2 behavioral symptoms index, internalizing, and externalizing problems T-Scores among children per ln-unit increase in maternal and paternal preconception and maternal prenatal urinary bisphenol A and ∑paraben concentrations 10

**Supplemental Figure 1**: Simplified Directed Acyclic Graph (DAG) for the association

of urinary BPA and ∑paraben metabolite concentrations with neurobehavior in children 11

**Supplemental Figure 2**: Adjusted differences in the BASC-2 behavioral symptoms index, internalizing, and externalizing problems T-Scores with loge-unit increase in maternal and paternal preconception and maternal prenatal urinary bisphenol A concentrations 12 **Supplemental Figure 3**: Adjusted differences in the BASC-2 behavioral symptoms index, internalizing, and externalizing problems T-Scores with loge-unit increase in maternal and paternal preconception and maternal prenatal urinary ∑paraben concentrations 13

**Supplemental Figure 4:** Adjusted differences in the BASC-2 behavioral symptoms index, internalizing, and externalizing T-Scores with ln-unit increase in maternal prenatal urinary BPA and ∑paraben concentrations 14

Supplemental Table 1: Baseline characteristics of the study participants and the original EARTH Study cohort

|  |  |  |
| --- | --- | --- |
|  | Mothers | Fathers |
| Parental Characteristic | Study sample | All EARTH participants | Study sample | All EARTH participants |
| N = 127 | N=799 | N = 93 | N=487 |
| Mean Age (years) | 34.8 | 34.7 | 35.9 | 36.6 |
| Race Percent (%) |  |  |  |  |
|  | White | 92 | 81 | 94 | 86 |
|  | Asian | 6 | 9 | 4 | 7 |
|  | Other | 2 | 10 | 2 | 7 |
| Mean BMI | 23.8 | 24.6 | 27.1 | 27.5 |
| Education Percent (%) |  |  |  |  |
|  | < College | 2 | 8 | 11 | 11 |
|  | College Graduate | 36 | 29 | 29 | 28 |
|  | Graduate Degree | 57 | 49 | 41 | 41 |
|  | Missing | 5 | 14 | 19 | 20 |
| Smoking Status Percent (%) |  |  |  |  |
|  | Never | 72 | 73 | 76 | 67 |
|  | Former/Current | 28 | 27 | 24 | 33 |

Supplemental Table 2: Distribution of specific gravity standardized preconception and prenatal urinary phenol concentrations in women and men in the EARTH study

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Phenol | Sample type | Sample Size (N) | LOD (μg/L) | % detect | SG-standardized GM (μg/L) | SG- standardized median (μg/L) | 25th - 75th (μg/L) |
| BPA | father preconception | 97 | 0.4 | 81 | 1.7 | 1.7 | 0.9 - 2.7 |
| mother preconception | 126 | 0.4 | 58 | 1.3 | 1.2 | 0.9 - 1.8 |
| mother prenatal | 121 | 0.4 | 62 | 1.3 | 1.2 | 0.8 – 1.8 |
| Butyl Paraben | father preconception | 93 | 0.1 | 22 | 0.4 | 0.2 | 0.1 - 0.6 |
| mother preconception | 119 | 0.1 | 55 | 1.8 | 1.2 | 0.5 - 6.9 |
| mother prenatal | 121 | 0.1 | 46 | 0.9 | 0.7 | 0.3 – 2.5 |
| Methyl Paraben | father preconception | 93 | 1.0 | 100 | 28 | 21 | 11 – 55 |
| mother preconception | 119 | 1.0 | 99 | 150 | 156 | 72 – 347 |
| mother prenatal | 121 | 1.0 | 100 | 106 | 112 | 43 - 267 |
| Propyl Paraben  | father preconception | 93 | 0.1 | 85 | 3.4 | 2.9 | 0.8 - 9.1 |
| mother preconception | 119 | 0.1 | 93 | 30 | 31 | 14 - 89 |
| mother prenatal | 121 | 0.1 | 99 | 19 | 19 | 6.9 - 64 |
| ∑Paraben | father preconception | 93 | N/A | N/A | 34 | 25 | 4.2 – 68 |
| mother preconception | 119 | N/A | N/A | 190 | 189 | 99 - 449 |
| mother prenatal | 121 | N/A | N/A | 131 | 141 | 51 - 353 |

Supplemental Table 3: Spearman correlation coefficients between parental urinary bisphenol A and ∑paraben concentrations before conception among women and men in the EARTH study

|  |  |  |  |
| --- | --- | --- | --- |
|  |  | BPA (r) | ∑Paraben (r) |
|  |  | Maternal Preconception | Maternal Prenatal | Paternal Preconception | Maternal Preconception | Maternal Prenatal | Paternal Preconception |
| BPA (r) | Maternal Preconception | - |  |  |  |  |  |
| Maternal Prenatal | 0.27 | - |  |  |  |  |
| Paternal Preconception | 0.21 | 0.13 | - |  |  |  |
| ∑Paraben (r) | Maternal Preconception | 0.10 | 0.17 | 0.06 | - |  |  |
| Maternal Prenatal | 0.03 | 0.15 | -0.06 | 0.54 | - |  |
| Paternal Preconception | -0.05 | -0.28 | -0.08 | 0.11 | 0.02 | - |

Supplemental Table 4: Adjusted mean differences in the BASC-2 behavioral symptoms index, internalizing, and externalizing problems T-Scores stratified by child sex with loge-unit increase in maternal and paternal preconception and maternal prenatal urinary bisphenol A and ∑paraben concentrationsa,b

|  |  |  |
| --- | --- | --- |
|  | BPA (μg/L) | ∑Paraben (μg/L) |
|  | N | GirlsBeta (95% CI) | N | Boys Beta (95% CI) | EMM p-value | N | GirlsBeta (95% CI) | N | Boys Beta (95% CI) | EMM p-value |
| Behavioral symptoms index |  |  |  |  |  |  |  |  |
|  Maternal preconception | 73 | 0.5 (-2.3, 3.7) | 79 | 1.6 (-1.3, 4.5) | 0.82 | 71 | 0.1 (-1.5, 1.7) | 73 | -0.6 (-1.7, 0.5) | 0.50 |
|  Paternal preconception | 56 | -1.2 (-4.4, 2.1) | 58 | -3.6 (-8.0, 0.9) | 0.76 | 55 | -0.7 (-2.3, 0.9) | 55 | -1.9 (-4.7, 0.8) | 0.44 |
|  Maternal prenatal | 70 | -0.4 (-2.3, 1.5) | 75 | -2.3 (-4.6, -0.1) | 0.41 | 70 | 0.3 (-1.0, 1.6) | 75 | 0.1 (-1.5, 1.7) | 0.88 |
| Internalizing problems |  |  |  |  |  |  |  |  |
|  Maternal preconception | 72 | 0.8 (-2.8, 4.3)  | 79 | 2.8 (-1.2, 6.8) | 0.78 | 70 | 0.6 (-1.5, 2.8) | 73 | -0.3 (-1.7, 1.1) | 0.46 |
|  Paternal preconception | 55 | -2.5 (-5.3, 0.4) | 57 | 1.1 (-1.4, 3.6) | 0.34 | 54 | -0.2 (-1.6, 1.2) | 54 | 0.5 (-1.6, 2.5) | 0.62 |
|  Maternal prenatal | 69 | -3.0 (-6.4, 0.4) | 75 | -0.3 (-2.7, 2.0) | 0.54 | 69 | -0.6 (-1.8, 0.7)  | 75 | -0.5 (-2.2, 1.3) | 0.91 |
| Externalizing problems |  |  |  |  |  |  |  |  |
|  Maternal preconception | 74 | 0.6 (-2.3, 3.4)  | 80 | 1.7 (-1.2, 4.5) | 0.79 | 72 | -0.3 (-1.9, 1.4) | 74 | -0.5 (-1.7, 0.7) | 0.82 |
|  Paternal preconception | 56 | 0.3 (-2.4, 3.0) | 58 | -0.5 (-2.9, 1.9) | 0.81 | 55 | -1.6 (-3.0, -0.2) | 55 | -1.0 (-3.0, 1.1) | 0.62 |
|  Maternal prenatal | 71 | -0.3 (-2.7, 2.0) | 76 | -2.4 (-4.3, -0.4) | 0.41 | 71 | -0.3 (-1.6, 1.0) | 76 | 0.0 (-1.4, 1.4) | 0.78 |

aAdjusted for maternal or paternal age, smoking status, and race

bEffect Measure Modification (EMM) p-values were calculated using a two-sample z-test with beta coefficients and variances from the sex-stratified models to determine sex-specific differences

Supplemental Table 5: Adjusted difference in the BASC-2 behavioral symptoms index, internalizing, and externalizing problems T-Scores among children younger than 6 years old per ln-unit increase in maternal and paternal preconception and maternal prenatal urinary bisphenol A and ∑paraben concentrationsa

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | N | BPA (μg/L)Beta (95% CI) | N | ∑Paraben (μg/L)Beta (95% CI) |
| Behavioral symptoms index |  |  |
|  Maternal preconception | 127 | 1.1 (-1.5, 3.8) | 127 | -0.2 (-1.2, 0.9) |
|  Paternal preconception | 93 | -1.8 (-4.0, 0.4) | 93 | -1.0 (-2.6, 0.5) |
|  Maternal prenatal | 121 | -1.4 (-3.0, 0.2) | 121 | 0.1 (-1.0, 1.1) |
| Internalizing problems |  |  |  |  |
|  Maternal preconception | 126  | 2.4 (-0.3, 5.1) | 126 | 0.0 (-1.2, 1.1) |
|  Paternal preconception | 91 | -1.0 (-3.0, 1.0) | 91 | -0.3 (-1.7, 1.1) |
|  Maternal prenatal | 120 | -0.2 (-1.9, 1.5) | 120 | -0.2 (-1.4, 1.0) |
| Externalizing problems |  |  |
|  Maternal preconception | 129  | 1.2 (-1.3, 3.6) | 129 | -0.3 (-1.5, 0.8) |
|  Paternal preconception | 93 | -1.1 (-3.1, 0.8) | 93  | -1.5 (-3.2, 0.1) |
|  Maternal prenatal | 123  | -1.1 (-2.7, 0.5) | 123 | -0.2 (-1.2, 0.9) |

aAdjusted for maternal or paternal age, smoking status, and race

Supplemental Table 6: Adjusted difference in the BASC-2 behavioral symptoms index, internalizing, and externalizing problems T-Scores among singleton children per ln-unit increase in maternal and paternal preconception and maternal prenatal urinary bisphenol A and ∑paraben concentrationsa

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | N | BPA (μg/L)Beta (95% CI) | N | ∑Paraben (μg/L)Beta (95% CI) |
| Behavioral symptoms index |  |  |
|  Maternal preconception | 101 | 1.8 (-0.9, 4.5) | 95 | -0.3 (-1.6, 1.0) |
|  Paternal preconception | 75 | -1.4 (-3.8, 1.0) | 71 | -0.9 (-2.4, 0.5) |
|  Maternal prenatal | 98 | -0.6 (-2.8, 1.6) | 98 | -0.2 (-1.4, 1.0) |
| Internalizing problems |  |  |  |  |
|  Maternal preconception | 101 | 1.0 (-1.8, 3.8) | 95 | -0.5 (-1.9, 0.8) |
|  Paternal preconception | 75 | -0.9 (-3.3, 1.4) | 71 | -0.1 (-1.5, 1.4) |
|  Maternal prenatal | 98 | -0.7 (-3.0, 1.6) | 98 | -0.6 (-1.8, 0.7) |
| Externalizing problems |  |  |
|  Maternal preconception | 101 | 2.3 (-0.5, 5.2) | 95 | -0.3 (-1.7, 1.1) |
|  Paternal preconception | 75 | -0.7 (-3.2, 1.7) | 71 | -1.5 (-3.0, -0.0) |
|  Maternal prenatal | 98 | -0.5 (-2.9, 1.8) | 98 | -0.5 (-1.7, 0.8) |

aAdjusted for maternal or paternal age, smoking status, and race

Supplemental Table 7: Adjusted difference in the BASC-2 behavioral symptoms index, internalizing, and externalizing problems T-Scores among children with a gestation > 37 weeks per ln-unit increase in maternal and paternal preconception and maternal prenatal urinary bisphenol A and ∑paraben concentrationsa

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | N | BPA (μg/L)Beta (95% CI) | N | ∑Paraben (μg/L)Beta (95% CI) |
| Behavioral symptoms index |  |  |
|  Maternal preconception | 117 | 1.9 (-0.6, 4.4) | 109 | -0.5 (-1.4, 0.5) |
|  Paternal preconception | 82 | -0.5 (-2.6, 1.6) | 79  | 0.1 (-0.9, 1.2) |
|  Maternal prenatal | 111 | -1.0 (-2.5, 0.5) | 111 | -0.6 (-1.7, 0.5) |
| Internalizing problems |  |  |  |  |
|  Maternal preconception | 117 | 1.5 (-1.2, 4.2) | 109 | -0.5 (-1.7, 0.7) |
|  Paternal preconception | 82  | 0.4 (-1.3, 2.1) | 79 | 0.4 (-1.0, 1.8) |
|  Maternal prenatal | 111 | -0.5 (-2.4, 1.4) | 111 | -0.6 (-1.8, 0.6) |
| Externalizing problems |  |  |
|  Maternal preconception | 117 | 2.1 (-0.1, 4.3) | 109 | -0.7 (-1.8, 0.4) |
|  Paternal preconception | 82 | -0.2 (-2.1, 1.7) | 79 | -0.6 (-1.8, 0.5) |
|  Maternal prenatal | 111 | -0.8 (-2.2, 0.6) | 111 | -0.9 (-1.9, 0.1) |

aAdjusted for maternal or paternal age, smoking status, and race

|  |  |  |  |
| --- | --- | --- | --- |
| Among… | Adjustments | N | Beta (95% CI) |
| All children | Unadjusted | 154 | 1.4 (-0.7, 3.5) |
| All children | maternal age, race, and smoking  | 154 | 1.2 (-0.9, 3.4) |
| Singletons | maternal age, race, and smoking  | 101 | 2.3 (-0.5, 5.2) |
| Children born term | maternal age, race, and smoking  | 117 | 2.1 (-0.1, 4.3) |
| Singleton children born term | maternal age, race, and smoking  | 87 | 2.6 (0.1, 5.2) |
| All children | maternal age, race, smoking, and education  | 121 | 1.8 (-0.2, 3.8) |
| Singletons | maternal age, race, smoking, and education  | 113 | 2.9 (0.8, 5.0) |
| Children born term | maternal age, race, smoking, and education  | 97 | 3.5 (1.1, 5.8) |
| Singleton children born term | maternal age, race, smoking, and education  | 83 | 3.7 (1.2, 6.1) |

Supplemental Table 8: Difference in externalizing problems t-score per ln-unit increase in maternal preconception urinary BPA concentration

\*-Term defined as >37 weeks gestation

Supplemental Table 9: Adjusted difference in the BASC-2 behavioral symptoms index, internalizing, and externalizing problems T-Scores among children per ln-unit increase in maternal and paternal preconception and maternal prenatal urinary bisphenol A and ∑paraben concentrations

|  |  |  |  |
| --- | --- | --- | --- |
|  | Fully Adjusted model: Adjusted for maternal or paternal age, smoking status, and race | Adjusted for maternal or paternal age, smoking status, race, and respective partner’s chemical preconception concentration | Adjusted for maternal or paternal age, smoking status, race, and person respective other chemical concentration |
|  | N | BPA (μg/L)Beta (95% CI) | N | ∑Paraben (μg/L)Beta (95% CI) | N | BPA (μg/L)Beta (95% CI) | N | ∑Paraben (μg/L)Beta (95% CI) | N | BPA (μg/L)Beta (95% CI) | N | ∑Paraben (μg/L)Beta (95% CI) |
| Behavioral symptoms index |  |  |  |  |  |  |  |  |  |  |
|  Maternal preconception | 152 | 1.0 (-1.4, 3.3) | 144 | -0.3 (-1.3, 0.7) | 110 | 1.0 (-1.9, 3.9) | 105 | 0.7 (-0.7, 2.1) | 144 | 1.3 (-1.2, 3.8) | 144 | -0.3 (-1.3, 0.7) |
|  Paternal preconception | 114 | -1.2 (-3.2, 0.8) | 110 | -0.6 (-1.8, 0.6) | 110 | -1.1 (-3.1, 0.9) | 105 | -0.4 (-1.6, 0.8) | 110 | -1.4 (-3.5, 0.7) | 110 | -1.2 (-2.5, 0.1) |
|  Maternal prenatal | 145 | -1.5 (-3.0, 0.0) | 145 | 0.1 (-0.9, 1.1) |  | N/A |  | N/A | 145 | -1.5 (-3, 0) | 145 | 0.2 (-0.7, 1.1) |
| Internalizing problems |  |  |  |  |  |  |  |  |  |  |  |
|  Maternal preconception | 151 | 1.1 (-1.4, 3.6) | 142 | -0.3 (-1.4, 0.8) | 108 | 0.6 (-2.9, 4.1) | 103 | 0.6 (-0.8, 2) | 143 | 1.9 (-0.7, 4.5) | 143 | -0.3 (-1.4, 0.8) |
|  Paternal preconception | 112 | -0.6 (-2.4, 1.2) | 108 | 0.0 (-1.2, 1.2) | 108 | -0.4 (-2.2, 1.4) | 103 | 0.1 (-1.1, 1.3) | 108 | -0.6 (-2.6, 1.4) | 108 | 0 (-1.2, 1.2) |
|  Maternal prenatal | 144 | -1.0 (-2.7, 0.7) | 144 | -0.5 (-1.5, 0.5) |  | N/A |  | N/A | 144 | 0.9 (-0.8, 2.6) | 144 | -0.4 (-1.4, 0.6) |
| Externalizing problems |  |  |  |  |  |  |  |  |  |  |
|  Maternal preconception | 154 | 1.2 (-0.9, 3.4) | 146 | -0.4 (-1.5, 0.7) | 110 | 0.5 (-2, 3) | 105 | 0.2 (-1.3, 1.7) | 146 | 1.6 (-0.7, 3.9) | 146 | -0.5 (-1.6, 0.6) |
|  Paternal preconception | 114 | -0.5 (-2.3, 1.2) | 110 | -1.2 (-2.5, 0.1) | 110 | -0.4 (-2.1, 1.3) | 105 | -1.1 (-2.3, 0.1) | 110 | -1.2 (-2.5, 0.1) | 110 | -0.7 (-1.9, 0.5) |
|  Maternal prenatal | 147 | -1.2 (-2.6, 0.2) | 147 | -0.2 (-1.1, 0.7) |  | N/A |  | N/A | 147 | -1.1 (-2.6, 0.4) | 147 | -0.1 (-1, 0.8) |

Supplemental Figure 1: Simplified Directed Acyclic Graph (DAG) for the association of urinary BPA and ∑paraben metabolite concentrations with neurobehavior in children



Supplemental Figure 2: Adjusted differences in the BASC-2 behavioral symptoms index, internalizing, and externalizing T-Scores with ln-unit increase in maternal and paternal preconception urinary bisphenol A concentrationsa



aFA is the fully adjusted model which included maternal or paternal age, smoking status, and race.

Supplemental Figure 3: Adjusted differences in the BASC-2 behavioral symptoms index, internalizing, and externalizing T-Scores with ln-unit increase in maternal and paternal preconception urinary ∑paraben concentrationsa



aFA is the fully adjusted model which included maternal or paternal age, smoking status, and race

Supplemental Figure 4: Adjusted differences in the BASC-2 behavioral symptoms index, internalizing, and externalizing T-Scores with ln-unit increase in maternal prenatal urinary BPA and ∑paraben concentrationsa



aFA is the fully adjusted model which included maternal or paternal age, smoking status, and race