

Title: Associations of Prenatal Urinary Phthalate Exposure with Preterm Birth: The Maternal-Infant Research on Environmental Chemicals (MIREC) Study

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Tables and Figures:

| | |
|---|----|
| Figure S1. Forest plots depicting the 95% confidence intervals based on a review of published studies. | 2 |
| Figure S2. Directed Acyclic Graph (DAG) for the relation among urinary phthalate metabolite concentrations during pregnancy, either gestational age (GA) or preterm birth (PTB), and various demographic characteristics. | 3 |
| Figure S3. Forest plots depicting the Hazard Ratios (HRs) and 95% confidence interval for preterm birth (PTB) and spontaneous preterm birth (sPTB) according to phthalate levels (quartiles). | 4 |
| Table S1. Hazard ratios (HRs) for preterm birth (PTB) and spontaneous preterm birth (sPTB) according to maternal demographic and pregnancy-related characteristics among MIREC study participants in Canada, 2008-2011, using Cox Proportional Hazards Regression. | 5 |
| Table S2. Hazard ratios (HRs) for preterm birth (PTB) or spontaneous preterm birth (sPTB) according to quartiles of urinary phthalate metabolite concentrations among MIREC study participants in Canada, 2008-2011, calculated using Cox Proportional Hazards Regression. | 7 |
| Table S3. Hazard ratios (HRs) for preterm birth (PTB) or spontaneous preterm birth (sPTB) according to 2-fold increase in urinary phthalate metabolite concentrations for infant boys among MIREC study participants in Canada, 2008-2011, calculated using Cox Proportional Hazards Regression. | 10 |
| Table S4. Hazard ratios (HRs) for preterm birth (PTB) or spontaneous preterm birth (sPTB) according to 2-fold increase in urinary phthalate metabolite concentrations for infant girls among MIREC study participants in Canada, 2008-2011, calculated using Cox Proportional Hazards Regression. | 11 |

Figure S1 C: Hazard ratios for Time-to-Delivery

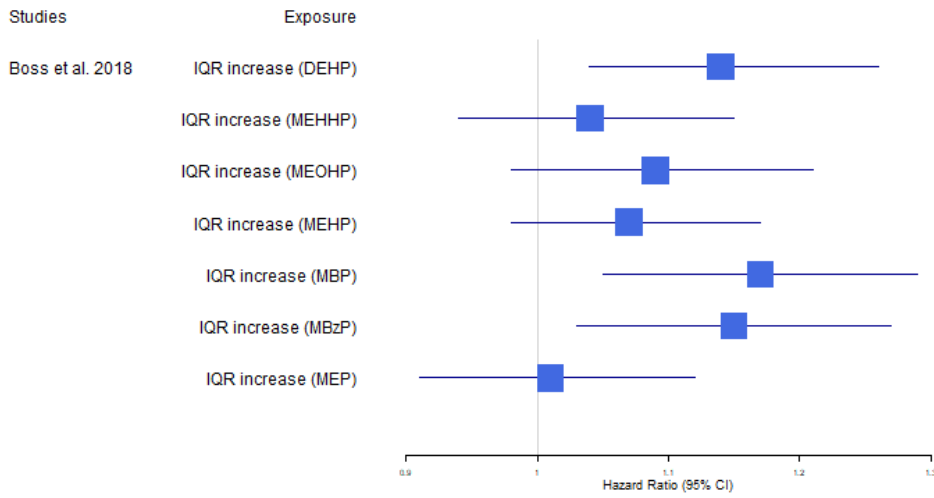


Figure S1. Forest plots depicting the 95% confidence intervals based on a review of published studies.

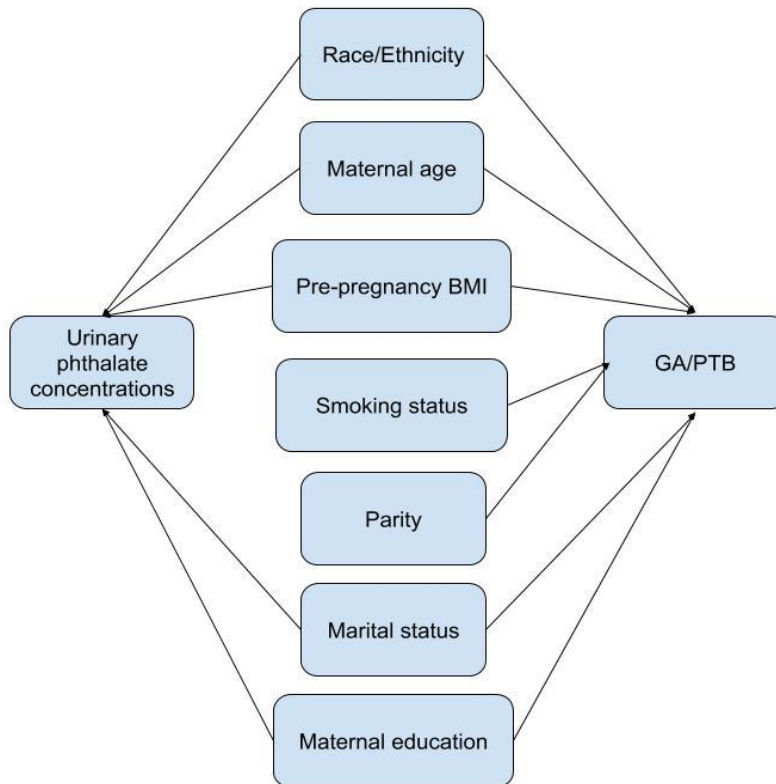


Figure S2. Directed Acyclic Graph (DAG) for the relation among urinary phthalate metabolite concentrations during pregnancy, either gestational age (GA) or preterm birth (PTB), and various demographic characteristics.

Figure S3 A: Hazard ratios for PTB

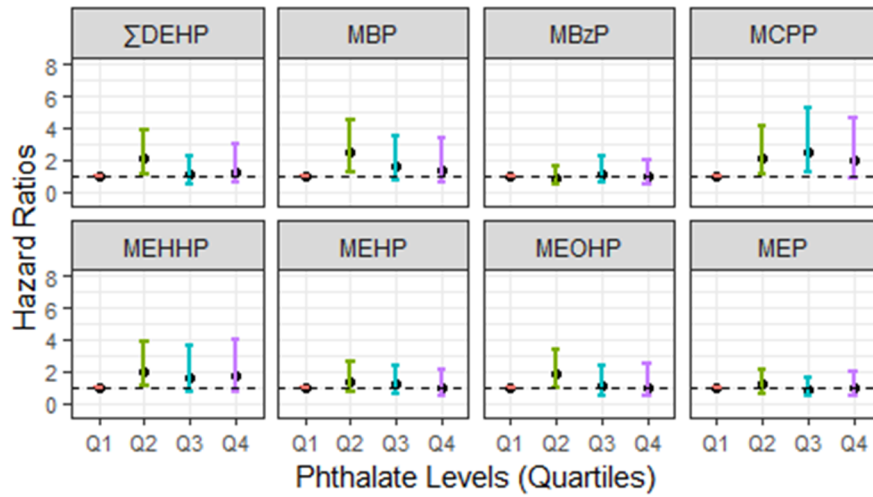


Figure S3 B: Hazard ratios for sPTB

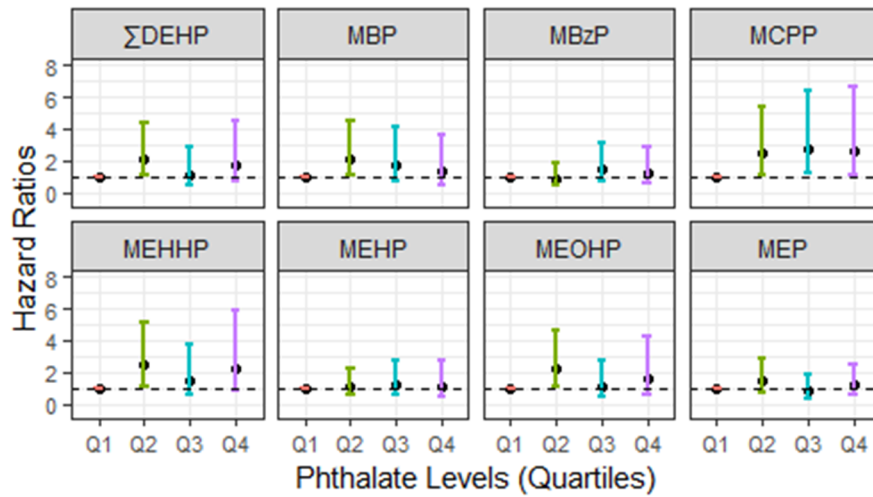


Figure S3. Forest plots depicting the Hazard Ratios (HRs) and 95% confidence interval for preterm birth (PTB) and spontaneous preterm birth (sPTB) according to phthalate levels (quartiles).

Table S1. Hazard ratios (HRs) for preterm birth (PTB) and spontaneous preterm birth (sPTB) according to maternal demographic and pregnancy-related characteristics among MIREC study participants in Canada, 2008-2011, using Cox Proportional Hazards Regression.

| | n (%) | HRs for PTB (Event = PTB) | | HRs for sPTB (Event = sPTB) | |
|---------------------------------|--------------|---------------------------|--------------------|-----------------------------|--------------------|
| | | Crude (95% CI) | Adjusted* (95% CI) | Crude (95% CI) | Adjusted* (95% CI) |
| Race | | | | | |
| Others | 340 (18.3%) | 1.19 (0.76, 1.86) | 1.17 (0.72, 1.91) | 1.12 (0.66, 1.91) | 1.05 (0.59, 1.88) |
| White | 1517 (81.7%) | referent | referent | referent | referent |
| Maternal Age | | | | | |
| ≤24 | 117 (6.3%) | 1.33 (0.64, 2.76) | 0.95 (0.38, 2.35) | 0.69 (0.25, 1.96) | 0.55 (0.18, 1.75) |
| 25-29 | 443 (24.0%) | 0.69 (0.39, 1.21) | 0.72 (0.40, 1.28) | 0.62 (0.33, 1.16) | 0.62 (0.33, 1.18) |
| 30-34 | 656 (35.5%) | referent | referent | referent | referent |
| 35-39 | 502 (27.2%) | 1.34 (0.86, 2.10) | 1.28 (0.80, 2.04) | 1.17 (0.71, 1.92) | 1.08 (0.63, 1.84) |
| 40+ | 127 (6.9%) | 1.37 (0.68, 2.74) | 1.42 (0.70, 2.89) | 0.80 (0.31, 2.05) | 0.80 (0.31, 2.08) |
| Marital Status | | | | | |
| Married | 1337 (72.0%) | referent | referent | referent | referent |
| Single | 78 (4.2%) | 1.32 (0.58, 3.03) | 1.54 (0.64, 3.73) | 1.37 (0.55, 3.40) | 1.72 (0.65, 4.59) |
| Same Partner ≥1yr | 432 (23.3%) | 1.20 (0.79, 1.84) | 1.23 (0.76, 1.98) | 0.91 (0.54, 1.55) | 0.94 (0.52, 1.70) |
| Others | 10 (0.5%) | 1.72 (0.24, 12.35) | 1.39 (0.19, 10.17) | 2.11 (0.29, 15.22) | 1.97 (0.26, 14.66) |
| Education Level | | | | | |
| High School Diploma or less | 161 (8.7%) | 1.26 (0.64, 2.47) | 0.96 (0.40, 2.31) | 1.29 (0.58, 2.83) | 1.53 (0.60, 3.95) |
| College or Trade School Diploma | 538 (29.0%) | 1.38 (0.88, 2.16) | 1.23 (0.75, 2.00) | 1.49 (0.89, 2.49) | 1.51 (0.86, 2.65) |
| Undergraduate University Degree | 681 (36.7%) | referent | referent | referent | referent |
| Graduate University Degree | 475 (25.6%) | 1.05 (0.64, 1.73) | 1.05 (0.63, 1.76) | 1.07 (0.60, 1.91) | 1.04 (0.57, 1.91) |
| Smoking Status | | | | | |
| Never | 1137 (61.3%) | referent | referent | referent | referent |
| Current | 106 (5.7%) | 0.91 (0.39, 2.09) | 1.17 (0.48, 2.89) | 0.82 (0.30, 2.27) | 1.00 (0.34, 3.01) |
| Former | 498 (26.8%) | 0.96 (0.63, 1.48) | 0.98 (0.63, 1.53) | 0.94 (0.57, 1.55) | 0.95 (0.56, 1.61) |
| Quit during Pregnancy | 115 (6.2%) | 1.13 (0.54, 2.35) | 1.13 (0.53, 2.41) | 1.31 (0.59, 2.87) | 1.35 (0.59, 3.08) |

| Parity | | | | | |
|---|--------------|-------------------|-------------------|-------------------|-------------------|
| 0 | 812 (43.7%) | referent | referent | referent | referent |
| 1 | 751 (40.4%) | 0.98 (0.66, 1.45) | 0.99 (0.65, 1.51) | 1.08 (0.68, 1.70) | 1.09 (0.67, 1.79) |
| 2 | 222 (12.0%) | 0.91 (0.50, 1.68) | 0.87 (0.45, 1.67) | 0.99 (0.49, 2.00) | 0.89 (0.42, 1.90) |
| 3+ | 72 (3.9%) | 0.65 (0.20, 2.07) | 0.55 (0.17, 1.81) | 0.64 (0.15, 2.65) | 0.56 (0.13, 2.39) |
| Pre-Pregnancy BMI | | | | | |
| Underweight | 49 (2.9%) | 0.82 (0.20, 3.37) | 0.90 (0.22, 3.71) | 1.03 (0.25, 4.26) | 1.06 (0.26, 4.43) |
| Normal | 1040 (60.5%) | referent | referent | referent | referent |
| Overweight | 372 (21.6%) | 1.08 (0.65, 1.82) | 1.10 (0.66, 1.86) | 0.96 (0.53, 1.72) | 0.94 (0.52, 1.71) |
| Obese | 258 (15.0%) | 2.67 (1.73, 4.13) | 2.72 (1.72, 4.32) | 1.82 (1.06, 3.11) | 1.67 (0.95, 2.94) |
| *Adjusted for other variables in the table. | | | | | |

Table S2. Hazard ratios (HRs) for preterm birth (PTB) or spontaneous preterm birth (sPTB) according to quartiles of urinary phthalate metabolite concentrations among MIREC study participants in Canada, 2008-2011, calculated using Cox Proportional Hazards Regression.

| Phthalates (quartiles) | Value (ug/L) | HRs for PTB (Event=PTB) | | | | HRs for sPTB (Event=sPTB) | | | |
|------------------------|--------------|-------------------------|-----|----------------------|---------------------|---------------------------|-----|----------------------|---------------------|
| | | #PTB | n | Unadjusted* (95% CI) | Adjusted** (95% CI) | #sPTB | n | Unadjusted* (95% CI) | Adjusted** (95% CI) |
| MBP | | | | | | | | | |
| Q1 | ≤5.1 | 17 | 421 | referent | referent | 15 | 414 | referent | referent |
| Q2 | >5.1 - ≤12 | 36 | 437 | 1.93 (1.05, 3.54) | 2.47 (1.26, 4.84) | 25 | 429 | 1.59 (0.81, 3.13) | 2.15 (1.04, 4.47) |
| Q3 | >12 - ≤25 | 25 | 415 | 1.24 (0.59, 2.60) | 1.57 (0.70, 3.51) | 21 | 406 | 1.31 (0.58, 2.94) | 1.70 (0.71, 4.08) |
| Q4 | >25 | 23 | 407 | 1.10 (0.48, 2.55) | 1.38 (0.56, 3.41) | 16 | 392 | 1.01 (0.39, 2.60) | 1.29 (0.47, 3.55) |
| MBzP | | | | | | | | | |
| Q1 | ≤2.3 | 26 | 434 | referent | referent | 20 | 426 | referent | referent |
| Q2 | >2.3 - ≤5.1 | 19 | 411 | 0.72 (0.39, 1.33) | 0.84 (0.44, 1.60) | 13 | 405 | 0.68 (0.33, 1.41) | 0.85 (0.40, 1.80) |
| Q3 | >5.1 - ≤12 | 29 | 426 | 1.02 (0.55, 1.89) | 1.12 (0.58, 2.16) | 23 | 414 | 1.21 (0.60, 2.43) | 1.46 (0.70, 3.06) |
| Q4 | >12 | 27 | 409 | 0.94 (0.48, 1.87) | 0.92 (0.44, 1.93) | 21 | 396 | 1.15 (0.53, 2.48) | 1.23 (0.54, 2.80) |
| MCP | | | | | | | | | |
| Q1 | ≤0.3 | 18 | 426 | referent | referent | 13 | 419 | referent | referent |
| Q2 | >0.3 - ≤0.92 | 26 | 417 | 1.50 (0.81, 2.79) | 2.06 (1.03, 4.12) | 21 | 404 | 1.80 (0.89, 3.67) | 2.45 (1.11, 5.38) |
| Q3 | >0.92 - ≤2.1 | 31 | 426 | 1.74 (0.89, 3.40) | 2.49 (1.20, 5.20) | 22 | 417 | 1.95 (0.90, 4.24) | 2.72 (1.17, 6.33) |

| | | | | | | | | | |
|--------------|-------------|----|-----|-------------------|-------------------|----|-----|-------------------|-------------------|
| Q4 | >2.1 | 26 | 411 | 1.51 (0.72, 3.19) | 2.00 (0.88, 4.56) | 21 | 401 | 2.03 (0.87, 4.74) | 2.61 (1.03, 6.65) |
| MEHHP | | | | | | | | | |
| Q1 | ≤4 | 19 | 422 | referent | referent | 14 | 416 | referent | referent |
| Q2 | >4 - ≤9.3 | 31 | 423 | 1.55 (0.85, 2.85) | 2.02 (1.04, 3.92) | 26 | 405 | 1.95 (0.98, 3.87) | 2.42 (1.15, 5.07) |
| Q3 | >9.3 - ≤20 | 25 | 433 | 1.17 (0.57, 2.39) | 1.64 (0.76, 3.56) | 16 | 432 | 1.13 (0.49, 2.63) | 1.50 (0.61, 3.69) |
| Q4 | >20 | 26 | 402 | 1.27 (0.58, 2.78) | 1.70 (0.72, 3.99) | 21 | 388 | 1.68 (0.69, 4.11) | 2.24 (0.85, 5.86) |
| MEHP | | | | | | | | | |
| Q1 | ≤1.0 | 24 | 434 | referent | referent | 19 | 425 | referent | referent |
| Q2 | >1 - ≤2.2 | 30 | 427 | 1.11 (0.63, 1.97) | 1.39 (0.76, 2.55) | 20 | 419 | 1.03 (0.53, 2.00) | 1.09 (0.54, 2.19) |
| Q3 | >2.2 - ≤4.4 | 24 | 408 | 0.83 (0.42, 1.63) | 1.16 (0.57, 2.37) | 19 | 395 | 1.00 (0.47, 2.13) | 1.23 (0.55, 2.75) |
| Q4 | >4.4 | 23 | 411 | 0.73 (0.35, 1.54) | 0.96 (0.44, 2.10) | 19 | 402 | 0.96 (0.42, 2.20) | 1.14 (0.48, 2.72) |
| MEOHP | | | | | | | | | |
| Q1 | ≤2.9 | 20 | 425 | referent | referent | 14 | 419 | referent | referent |
| Q2 | >2.9 - ≤6.4 | 35 | 418 | 1.57 (0.87, 2.83) | 1.80 (0.95, 3.39) | 29 | 407 | 2.09 (1.06, 4.11) | 2.25 (1.10, 4.62) |
| Q3 | >6.4 - ≤13 | 22 | 423 | 0.85 (0.41, 1.77) | 1.09 (0.50, 2.38) | 14 | 414 | 0.94 (0.40, 2.25) | 1.12 (0.45, 2.78) |
| Q4 | >13 | 24 | 414 | 0.86 (0.38, 1.94) | 1.02 (0.43, 2.44) | 20 | 401 | 1.36 (0.55, 3.40) | 1.58 (0.60, 4.19) |
| MEP | | | | | | | | | |
| Q1 | ≤11 | 23 | 431 | referent | referent | 17 | 424 | referent | referent |

| | | | | | | | | | |
|--|----------------------|----|-----|-------------------|-------------------|----|-----|-------------------|-------------------|
| Q2 | >11 - ≤28 | 30 | 413 | 1.27 (0.71, 2.26) | 1.16 (0.63, 2.13) | 24 | 404 | 1.48 (0.76, 2.85) | 1.41 (0.71, 2.81) |
| Q3 | >28 - ≤86 | 21 | 420 | 0.85 (0.45, 1.61) | 0.83 (0.42, 1.63) | 15 | 404 | 0.91 (0.43, 1.91) | 0.84 (0.38, 1.85) |
| Q4 | >86.1 | 27 | 416 | 1.09 (0.58, 2.04) | 1.01 (0.51, 1.97) | 21 | 409 | 1.26 (0.61, 2.59) | 1.16 (0.53, 2.50) |
| ΣDEHP | | | | | | | | | |
| Q1 | ≤0.0281 | 20 | 420 | referent | referent | 15 | 411 | referent | referent |
| Q2 | >0.0281 - ≤0.0625 | 36 | 420 | 1.60 (0.89, 2.88) | 2.04 (1.07, 3.85) | 27 | 410 | 1.77 (0.90, 3.47) | 2.13 (1.04, 4.38) |
| Q3 | >0.0625 - ≤0.129 | 19 | 420 | 0.74 (0.35, 1.56) | 1.02 (0.46, 2.26) | 14 | 410 | 0.88 (0.38, 2.05) | 1.13 (0.46, 2.79) |
| Q4 | >0.129 | 26 | 420 | 0.94 (0.42, 2.06) | 1.24 (0.53, 2.91) | 21 | 410 | 1.30 (0.53, 3.17) | 1.70 (0.65, 4.43) |
| * Adjusted for specific gravity | | | | | | | | | |
| ** Adjusted for specific gravity, maternal age, race, education, pre-pregnancy BMI, smoking status, marital status, parity | | | | | | | | | |

Table S3. Hazard ratios (HRs) for preterm birth (PTB) or spontaneous preterm birth (sPTB) according to 2-fold increase in urinary phthalate metabolite concentrations for infant boys among MIREC study participants in Canada, 2008-2011, calculated using Cox Proportional Hazards Regression.

| Phthalates (2-fold increase in exposure) | HRs for PTB (Event=PTB) | | HRs for sPTB (Event=sPTB) | |
|--|-------------------------|---------------------|---------------------------|---------------------|
| | Unadjusted* (95% CI) | Adjusted** (95% CI) | Unadjusted* (95% CI) | Adjusted** (95% CI) |
| MBP | 1.00 (0.81, 1.24) | 1.03 (0.83, 1.29) | 1.03 (0.82, 1.30) | 1.06 (0.84, 1.36) |
| MBzP | 0.97 (0.81, 1.16) | 0.97 (0.80, 1.17) | 0.96 (0.79, 1.18) | 0.97 (0.79, 1.19) |
| MCPP | 1.15 (0.99, 1.34) | 1.10 (0.93, 1.29) | 1.29 (1.10, 1.51) | 1.19 (1.00, 1.41) |
| MEHHP | 1.02 (0.84, 1.23) | 1.04 (0.85, 1.27) | 1.10 (0.90, 1.33) | 1.09 (0.88, 1.34) |
| MEHP | 0.93 (0.75, 1.14) | 0.94 (0.75, 1.17) | 0.97 (0.77, 1.21) | 0.94 (0.74, 1.20) |
| MEOHP | 0.99 (0.80, 1.22) | 0.99 (0.80, 1.24) | 1.07 (0.87, 1.33) | 1.06 (0.84, 1.33) |
| MEP | 0.98 (0.86, 1.12) | 1.00 (0.87, 1.15) | 1.00 (0.86, 1.15) | 1.02 (0.87, 1.18) |
| ΣDEHP | 1.00 (0.82, 1.23) | 1.02 (0.82, 1.26) | 1.08 (0.88, 1.33) | 1.07 (0.85, 1.34) |

* Adjusted for specific gravity
** Adjusted for specific gravity, maternal age, race, education, pre-pregnancy BMI, smoking status, marital status, parity

Table S4. Hazard ratios (HRs) for preterm birth (PTB) or spontaneous preterm birth (sPTB) according to 2-fold increase in urinary phthalate metabolite concentrations for infant girls among MIREC study participants in Canada, 2008-2011, calculated using Cox Proportional Hazards Regression.

| Phthalates (2-fold increase in exposure) | HRs for PTB (Event=PTB) | | HRs for sPTB (Event=sPTB) | |
|--|-------------------------|---------------------|---------------------------|---------------------|
| | Unadjusted* (95% CI) | Adjusted** (95% CI) | Unadjusted* (95% CI) | Adjusted** (95% CI) |
| MBP | 0.93 (0.73, 1.18) | 0.93 (0.72, 1.19) | 0.91 (0.68, 1.21) | 0.91 (0.69, 1.21) |
| MBzP | 1.02 (0.83, 1.25) | 1.02 (0.81, 1.27) | 1.07 (0.84, 1.36) | 1.10 (0.84, 1.43) |
| MCPP | 0.93 (0.76, 1.15) | 0.98 (0.80, 1.21) | 0.80 (0.62, 1.05) | 0.85 (0.65, 1.13) |
| MEHHP | 0.95 (0.76, 1.19) | 0.97 (0.76, 1.24) | 0.96 (0.74, 1.26) | 1.00 (0.75, 1.34) |
| MEHP | 0.92 (0.73, 1.14) | 0.95 (0.75, 1.21) | 0.98 (0.76, 1.27) | 1.02 (0.77, 1.34) |
| MEOHP | 0.96 (0.76, 1.22) | 0.99 (0.76, 1.27) | 1.00 (0.76, 1.32) | 1.04 (0.77, 1.40) |
| MEP | 1.03 (0.90, 1.19) | 0.99 (0.85, 1.16) | 1.04 (0.88, 1.23) | 0.98 (0.81, 1.19) |
| ΣDEHP | 0.94 (0.74, 1.19) | 0.97 (0.75, 1.25) | 0.97 (0.73, 1.28) | 1.01 (0.75, 1.37) |

* Adjusted for specific gravity
** Adjusted for specific gravity, maternal age, race, education, pre-pregnancy BMI, smoking status, marital status, parity