**Supplemental Information**

**Maternal Urinary Metal and Metalloid levels in Association with Oxidative Stress Biomarkers in Northern Puerto Rico**

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Table 1. Percent change in urinary 8-iso-PGF2α, 8-iso-PGF2α metabolite, PGF2α, 8-iso-PGF2α chemical fraction, and 8-iso-PGF2α enzymaticfraction associated with exposure biomarker concentration. Effect estimates presented as percent changes for IQR increase in exposure biomarker concentration. Models were adjusted for specific gravity, study visit, maternal age, maternal education, marital status, pre-pregnancy BMI, and exposure to secondhand smoking.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Metals** | **8-iso-PGF2α** | | **8-iso-PGF2α metabolite** | | **PGF2α** | | **8-iso-PGF2α**  **chemical fraction** | | **8-iso-PGF2α**  **enzymatic fraction** | |
|  | **%Δ (95% CI)** | **p value** | **%Δ (95% CI)** | **p value** | **%Δ (95% CI)** | **p value** | **%Δ (95% CI)** | **p value** | **%Δ (95% CI)** | **p value** |
| *Essential Metals* | |  |  |  |  |  |  |  |  |  |
| Co | **7.8 (1.0, 15.1)** | **0.03\*** | 3.7 (-3.5, 11.4) | 0.32 | 6.8 (-2, 16.4) | 0.14 | **9.3 (0.9, 18.3)** | **0.03\*** | 7.6 (-23.6, 51.6) | 0.67 |
| Cs | **11.1 (4.5, 18.2)** | **0.001\*** | 6.6 (-0.5, 14.2) | 0.07 | **9.4 (0.8, 18.7)** | **0.03\*** | **14.5 (6.3, 23.4)** | **0.001\*** | **41.6 (2.5, 95.7)** | **0.04\*** |
| Cu | **14.9 (7.2, 23.2)** | **<0.001\*** | **9.4 (1.1, 18.3)** | **0.03\*** | 9.5 (-0.2, 20.1) | 0.06 | **19.7 (10.0, 30.3)** | **<0.001\*** | -5.3 (-34.6, 37.1) | 0.77 |
| Mn | 4.0 (-1.4, 9.6) | 0.16 | -0.7 (-6.3, 5.3) | 0.82 | -1.4 (-8.0, 5.7) | 0.70 | **7.1 (0.4, 14.2)** | **0.04\*** | -20.0 (-39.2, 5.4) | 0.12 |
| Mo | 6.0 (-1.5, 14.1) | 0.12 | 5.4 (-2.7, 14.2) | 0.20 | 5.8 (-3.9, 16.5) | 0.25 | 6.9 (-2.2, 16.9) | 0.14 | 15.1 (-21.5, 68.7) | 0.47 |
| Sb | **7.3 (0.2, 14.8)** | **0.05\*** | 6.5 (-1.1, 14.7) | 0.10 | 4.8 (-4.1, 14.7) | 0.30 | **10.4 (1.6, 19.8)** | **0.02\*** | 19.2 (-16.5, 70.0) | 0.34 |
| Sn | 6.3 (-0.5, 13.4) | 0.07 | -1.9 (-8.8, 5.6) | 0.61 | 4.5 (-4.0, 13.7) | 0.32 | 7.9 (-0.4, 16.8) | 0.07 | 4.0 (-25.9, 46.1) | 0.82 |
| Zn | **8.4 (1.2, 16.2)** | **0.02\*** | **8.2 (0.3, 16.7)** | **0.04\*** | **13.1 (3.4, 23.7)** | **0.01\*** | 7.5 (-1.2, 16.9) | 0.10 | **53.6 (7.4, 120)** | **0.02\*** |
| *Non-essential Metals* | |  |  |  |  |  |  |  |  |  |
| As | 3.9 (-3.6, 12.0) | 0.32 | -0.2 (-8.1, 8.4) | 0.97 | 3.8 (-5.9, 14.6) | 0.46 | 4.1 (-5.0, 14.1) | 0.39 | 2.9 (-30.4, 52.3) | 0.88 |
| Ba | 2.7 (-3.7, 9.6) | 0.42 | -1.9 (-8.6, 5.3) | 0.60 | 3.7 (-4.9, 13.0) | 0.42 | 3.0 (-4.8, 11.5) | 0.47 | 19.7 (-14.7, 68) | 0.30 |
| Cd | 0.5 (-5.5, 6.8) | 0.88 | 1.6 (-5.1, 8.7) | 0.66 | -1.5 (-9.2, 6.8) | 0.71 | 1.9 (-5.4, 9.8) | 0.62 | -6.4 (-31.9, 28.7) | 0.69 |
| Hg | -0.5 (-7.4, 7) | 0.90 | -4.0 (-11.3, 3.9) | 0.31 | 0.2 (-8.8, 10.0) | 0.97 | -0.3 (-8.7, 8.9) | 0.95 | 15.8 (-20.4, 68.4) | 0.44 |
| Ni | **8.2 (1.2, 15.6)** | **0.02\*** | 2.3 (-4.9, 10.1) | 0.54 | 5.5 (-3.3, 15.2) | 0.23 | **11.0 (2.4, 20.3)** | **0.01\*** | 8.8 (-23.2, 54.2) | 0.64 |
| Pb | 4.6 (-5.0, 15.2) | 0.36 | -6.9 (-16.1, 3.3) | 0.18 | -2.5 (-14.1, 10.7) | 0.70 | 9.4 (-2.7, 22.9) | 0.14 | -12.2 (-46.8, 45.0) | 0.61 |

Abbreviations: cobalt (Co); cesium (Cs); copper (Cu); manganese (Mn); molybdenum (Mo); antimony (Sb); tin (Sn); zinc (Zn); arsenic (As); barium (Ba); cadmium (Cd); mercury (Hg); nickel (Ni); lead (Pb).

\* denotes p < 0.05; **\***denotes p < 0.05 & q value (false discovery rate) <0.05.

Table 2. Percent change in urinary 8-iso-PGF2α, 8-iso-PGF2α metabolite, PGF2α, 8-iso-PGF2α chemical fraction, and 8-iso-PGF2α enzymatic fraction associated with urinary metal biomarker concentration at each visit during pregnancy. Effect estimates presented as percent changes (%) for IQR increase in exposure biomarker concentrationa. Models were adjusted for study visit, maternal age, maternal education, marital status, pre-pregnancy BMI, and exposure to secondhand smoking.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Metals** | **8-iso-PGF2α** | | | | | | **8-iso-PGF2α metabolite** | | | | | |
|  | **Visit 1** | | **Visit 2** | | **Visit 3** | | **Visit 1** | | **Visit 2** | | **Visit 3** | |
|  | %Δ (95% CI) | *p* value | %Δ (95% CI) | *p* value | %Δ (95% CI) | *p* value | %Δ (95% CI) | *p* value | %Δ (95% CI) | *p* value | %Δ (95% CI) | *p* value |
| *Essential metals* | |  |  |  |  |  |  |  |  |  |  |  |
| Co | 3.7 (-4.7, 12.9) | 0.40 | **11.1 (0.3, 23.2)** | **0.05\*** | 10.6 (-2.4, 25.3) | 0.12 | 0.5 (-8.4, 10.2) | 0.92 | 10.4 (-1.3, 23.5) | 0.09 | -0.5 (-13.5, 14.3) | 0.94 |
| Cs | 7.7 (-0.8, 16.8) | 0.08 | **12.0 (2.9, 21.8)** | **0.01\*** | **10.9 (2.1, 20.5)** | **0.02\*** | 1.4 (-7.2, 10.7) | 0.77 | **13.3 (3.4, 24.2)** | **0.01\*** | 4.8 (-4.9, 15.4) | 0.34 |
| Cu | **12.2 (1.7, 23.7)** | **0.02\*** | **15.3 (4.8, 26.8)** | **0.004\*** | **18.8 (4.9, 34.4)** | **0.01\*** | 0.7 (-9.5, 12.1) | 0.90 | **15.2 (3.9, 27.8)** | **0.01\*** | 15.6 (-0.5, 34.1) | 0.06 |
| Mn | 0.6 (-6.3, 8.0) | 0.87 | **9.7 (0.6, 19.7)** | **0.04\*** | 6.5 (-2.7, 16.6) | 0.17 | -4.2 (-11.3, 3.4) | 0.27 | 5.4 (-4.1, 16.0) | 0.28 | 2.3 (-7.7, 13.2) | 0.67 |
| Mo | 6.1 (-5.5, 19.2) | 0.32 | 5.8 (-4.0, 16.5) | 0.26 | 4.4 (-5.0, 14.8) | 0.37 | 2.4 (-9.7, 16.0) | 0.72 | 8.4 (-2.5, 20.4) | 0.14 | 3.7 (-6.6, 15.2) | 0.49 |
| Sb | 10.6 (-0.5, 22.9) | 0.06 | 4.0 (-4.9, 13.7) | 0.40 | 5.4 (-3.5, 15.2) | 0.25 | 5.3 (-6.1, 18.2) | 0.38 | 7.7 (-2.3, 18.7) | 0.14 | 4.1 (-5.6, 14.8) | 0.42 |
| Sn | 2.1 (-6.6, 11.8) | 0.64 | 6.1 (-2.8, 15.8) | 0.19 | 11.6 (-0.1, 24.6) | 0.05 | -5.4 (-14.3, 4.4) | 0.27 | 1.3 (-8.7, 12.3) | 0.81 | 0.8 (-10.9, 14.0) | 0.90 |
| Zn | **11.4 (0.8, 23.1)** | **0.04\*** | 6.0 (-4.1, 17.2) | 0.26 | 5.5 (-5.7, 17.9) | 0.35 | 0.7 (-9.6, 12.2) | 0.90 | **13.6 (2.0, 26.6)** | **0.02\*** | 11.6 (-1.6, 26.7) | 0.09 |
| *Non-essential metals* | |  |  |  |  |  |  |  |  |  |  |  |
| As | 4.3 (-6.3, 16.0) | 0.44 | 0.2 (-10.4, 12.0) | 0.98 | 6.3 (-4.8, 18.7) | 0.28 | -3.9 (-14.4, 7.8) | 0.50 | 8.0 (-4.4, 22.0) | 0.22 | -3.6 (-14.9, 9.2) | 0.56 |
| Ba | 7.7 (-4, 20.8) | 0.21 | 4.6 (-5.2, 15.4) | 0.37 | -5.2 (-16.0, 7.0) | 0.39 | 3.6 (-8.4, 17.3) | 0.57 | 3.1 (-7.3, 14.6) | 0.58 | **-14.4 (-24.9, -2.4)** | **0.02\*** |
| Cd | 8.0 (-3.7, 21.2) | 0.19 | -0.2 (-9.8, 10.5) | 0.97 | -6.1 (-18.8, 8.5) | 0.39 | -0.5 (-12.2, 12.8) | 0.94 | 3.9 (-7.0, 16.1) | 0.50 | -0.1 (-15.5, 18.2) | 0.99 |
| Hg | 0.2 (-10.5, 12.1) | 0.98 | 4.1 (-6.5, 15.9) | 0.47 | -5.9 (-16.1, 5.7) | 0.31 | -2.7 (-13.9, 9.9) | 0.66 | -1.6 (-12.7, 10.8) | 0.78 | -7.7 (-18.6, 4.8) | 0.22 |
| Ni | 6.9 (-2.8, 17.6) | 0.17 | 9.0 (-1.5, 20.7) | 0.10 | 7.1 (-2.9, 18.2) | 0.17 | -1.2 (-11.0, 9.7) | 0.82 | 4.4 (-6.7, 16.7) | 0.45 | 4.0 (-7.0, 16.3) | 0.49 |
| Pb | 3.6 (-9.7, 18.9) | 0.62 | 4.6 (-10.5, 22.2) | 0.57 | 6.1 (-11.6, 27.4) | 0.53 | -12.6 (-24.6, 1.4) | 0.08 | 4.2 (-11.9, 23.2) | 0.63 | -10.7 (-26.7, 8.8) | 0.27 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | **PGF2α** | | | | | | **8-iso-PGF2α chemical fraction** | | | | | |
|  | **Visit 1** | | **Visit 2** | | **Visit 3** | | **Visit 1** | | **Visit 2** | | **Visit 3** | |
|  | %Δ (95% CI) | *p* value | %Δ (95% CI) | *p* value | %Δ (95% CI) | *p* value | %Δ (95% CI) | *p* value | %Δ (95% CI) | *p* value | %Δ (95% CI) | *p* value |
| *Essential metals* | |  |  |  |  |  |  |  |  |  |  |  |
| Co | 0.0 (-10.6, 11.8) | 1.00 | 12.5 (-1.7, 28.9) | 0.09 | 11.6 (-5.5, 31.9) | 0.20 | 7.2 (-3.3, 18.8) | 0.19 | 10.7 (-2.3, 25.5) | 0.11 | 11.2 (-4.5, 29.5) | 0.18 |
| Cs | 2.3 (-8.3, 14.0) | 0.69 | **13.2 (1.2, 26.6)** | **0.03\*** | 11.6 (0.0, 24.7) | 0.05 | **13.5 (2.8, 25.2)** | **0.01\*** | **12.9 (2.0, 25.0)** | **0.02\*** | **12.3 (1.6, 24.1)** | **0.02\*** |
| Cu | 2.5 (-10.0, 16.9) | 0.71 | **14.2 (0.6, 29.8)** | **0.04\*** | 13.1 (-4.2, 33.4) | 0.15 | **19.9 (6.5, 35.0)** | **0.003\*** | **16.9 (4.2, 31.1)** | **0.01\*** | **24.1 (6.9, 44.0)** | **0.01\*** |
| Mn | -6.1 (-14.6, 3.2) | 0.19 | 5.2 (-6.2, 17.9) | 0.39 | 3.6 (-8.1, 16.8) | 0.57 | 4.9 (-3.8, 14.4) | 0.28 | **11.4 (0.2, 23.8)** | **0.05\*** | 7.9 (-3.3, 20.4) | 0.18 |
| Mo | 6.0 (-9.0, 23.5) | 0.46 | 10.9 (-2.3, 26.0) | 0.11 | -0.7 (-12.5, 12.6) | 0.91 | 5.2 (-8.5, 21.1) | 0.48 | 3.9 (-7.6, 16.8) | 0.52 | 9.5 (-2.4, 22.8) | 0.12 |
| Sb | -0.9 (-13.8, 14.0) | 0.90 | 6.5 (-5.5, 20.0) | 0.31 | 6.7 (-5.1, 20.1) | 0.28 | **20.6 (6.2, 36.9)** | **0.005\*** | 3.3 (-7.3, 15.0) | 0.56 | 6.3 (-4.5, 18.2) | 0.26 |
| Sn | -3.9 (-14.6, 8.1) | 0.51 | 4.4 (-7.0, 17.1) | 0.47 | **19.3 (3.1, 38.1)** | **0.02\*** | 7.8 (-3.4, 20.3) | 0.18 | 6.5 (-4.3, 18.4) | 0.25 | 7.3 (-6.2, 22.7) | 0.31 |
| Zn | 12.1 (-1.6, 27.7) | 0.09 | **14.2 (0.1, 30.3)** | **0.05\*** | 10.5 (-4.7, 28.1) | 0.19 | 12.9 (0.0, 27.4) | 0.05 | 2.3 (-9.5, 15.5) | 0.72 | 5.0 (-8.3, 20.2) | 0.48 |
| *Non-essential metals* | |  |  |  |  |  |  |  |  |  |  |  |
| As | 5.2 (-8.6, 21.1) | 0.48 | 2.2 (-11.7, 18.4) | 0.77 | 2.9 (-11.2, 19.2) | 0.71 | 3.4 (-9.2, 17.7) | 0.61 | -0.9 (-13.5, 13.5) | 0.90 | 9.0 (-4.6, 24.7) | 0.21 |
| Ba | -0.7 (-14.7, 15.6) | 0.92 | 9.5 (-3.8, 24.7) | 0.17 | -0.4 (-15.2, 16.9) | 0.96 | 13.7 (-1.1, 30.7) | 0.07 | 2.8 (-8.7, 15.9) | 0.65 | -7.5 (-20.2, 7.1) | 0.30 |
| Cd | 2.6 (-11.9, 19.4) | 0.74 | 1.2 (-11.6, 15.9) | 0.86 | -11.6 (-27, 7.0) | 0.21 | 13.0 (-1.7, 29.9) | 0.09 | -0.9 (-12.4, 12.0) | 0.88 | -3.5 (-19.0, 15.0) | 0.69 |
| Hg | -3.9 (-17.2, 11.5) | 0.60 | 5.3 (-8.6, 21.3) | 0.48 | -0.7 (-14.8, 15.7) | 0.92 | 3.9 (-9.3, 19.0) | 0.59 | 5.0 (-7.9, 19.6) | 0.47 | -9.7 (-21.5, 3.8) | 0.15 |
| Ni | -2.8 (-14.2, 10.1) | 0.66 | **15.2 (0.7, 31.7)** | **0.04\*** | 5.4 (-7.4, 20.0) | 0.43 | **14.5 (2.0, 28.5)** | **0.02\*** | 6.2 (-6.1, 20.1) | 0.34 | 9.4 (-2.8, 23.2) | 0.14 |
| Pb | -9.1 (-24.1, 8.9) | 0.30 | 6.2 (-13.4, 30.4) | 0.56 | -2.0 (-23, 24.8) | 0.87 | 12.1 (-5.1, 32.5) | 0.18 | 3.4 (-14.4, 24.9) | 0.73 | 12.4 (-9.9, 40.2) | 0.30 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | **8-iso-PGF2α enzymatic fraction** | | | | | |  |  |  |  |  |  |
|  | **Visit 1** | | **Visit 2** | | **Visit 3** | |  |  |  |  |  |  |
|  | %Δ (95% CI) | *p* value | %Δ (95% CI) | *p* value | %Δ (95% CI) | *p* value |  |  |  |  |  |  |
| *Essential metals* | |  |  |  |  |  |  |  |  |  |  |  |
| Co | -11.2 (-43, 38.2) | 0.60 | 8.5 (-36.6, 85.8) | 0.77 | 55.8 (-19.3, 201) | 0.19 |  |  |  |  |  |  |
| Cs | 8.8 (-29.0, 66.8) | 0.70 | 53.6 (-1.2, 139) | 0.06 | **62.1 (5.1, 150)** | **0.03\*** |  |  |  |  |  |  |
| Cu | -22.8 (-54.1, 29.8) | 0.33 | 0.8 (-39.1, 66.9) | 0.98 | 23.9 (-35.5, 138) | 0.52 |  |  |  |  |  |  |
| Mn | -20.5 (-45.2, 15.4) | 0.23 | -20.0 (-49.2, 25.8) | 0.34 | -18.7 (-49.2, 30.2) | 0.39 |  |  |  |  |  |  |
| Mo | -28.5 (-60.6, 29.8) | 0.27 | 57.4 (-4.2, 157) | 0.08 | 22.6 (-24.6, 99.5) | 0.41 |  |  |  |  |  |  |
| Sb | -11.4 (-49.0, 53.8) | 0.67 | 24 (-22.4, 98.2) | 0.37 | 38.1 (-13.1, 120) | 0.18 |  |  |  |  |  |  |
| Sn | 4.0 (-35.0, 66.4) | 0.87 | -12.9 (-44.9, 37.6) | 0.56 | 36.9 (-23.3, 144) | 0.29 |  |  |  |  |  |  |
| Zn | 24.6 (-25.6, 109) | 0.40 | **83.7 (9.5, 208)** | **0.02\*** | 52.7 (-14.1, 172) | 0.15 |  |  |  |  |  |  |
| *Non-essential metals* | |  |  |  |  |  |  |  |  |  |  |  |
| As | -12.1 (-49.6, 53.4) | 0.65 | 7.6 (-39.8, 92.4) | 0.81 | 16.8 (-34.3, 108) | 0.60 |  |  |  |  |  |  |
| Ba | -21.5 (-56.8, 42.6) | 0.43 | 47.8 (-11.3, 146) | 0.14 | 35.3 (-28.0, 154) | 0.35 |  |  |  |  |  |  |
| Cd | -20.4 (-56.2, 44.8) | 0.46 | 18.2 (-30.4, 101) | 0.54 | -30.7 (-67.4, 47.1) | 0.34 |  |  |  |  |  |  |
| Hg | 21.7 (-32.3, 119) | 0.51 | 15.2 (-34.2, 102) | 0.62 | 9.6 (-40.1, 100) | 0.77 |  |  |  |  |  |  |
| Ni | -22.4 (-52.8, 27.5) | 0.32 | 30.9 (-22.9, 122) | 0.32 | 30.7 (-21.6, 118) | 0.31 |  |  |  |  |  |  |
| Pb | -32.8 (-67.1, 37.4) | 0.28 | 11.5 (-50.4, 151) | 0.79 | 2.3 (-60.5, 165) | 0.96 |  |  |  |  |  |  |

Abbreviations: cobalt (Co); cesium (Cs); copper (Cu); manganese (Mn); molybdenum (Mo); antimony (Sb); tin (Sn); zinc (Zn); arsenic (As); barium (Ba); cadmium (Cd); mercury (Hg); nickel (Ni); lead (Pb).

\* denotes p < 0.05

\*denotes p < 0.05 & q value (false discovery rate) <0.05