## Table 1. Descriptive statistics of sample population

|  |  |  | n (%) or median (IQR) |
| --- | --- | --- | --- |
| Child |  | Female | 761 (49%) |
|  | Urinary F2-isoprostanes (ng/mg creatinine; Year 1) | iPF(2a)-III | -0.42 (-0.72, -0.09) |
|  |  | 2,3-dinor-iPF(2a)-III | 1.76 (1.55, 1.97) |
|  |  | iPF(2a-VI | 2.57 (2.31, 2.87) |
|  |  | 8,12-iso-iPF(2a)-VI | 2.58 (2.17, 2.91) |
|  | Salivary cortisol reactivity (ug/dl; Year 2) | Change between pre- and post-stressor cortisol | 0 (0, 0.01) |
|  |  | Cortisol residualized gain score | -0.09 (-0.21, 0.14) |
|  | sAA reactivity (U/ml; Year 2) | Change between pre- and post-stressor sAA | 1.41 (-0.08, 4.41) |
|  |  | sAA residualized gain score | -25.83 (-51.4, 28.68) |
|  | SAM biomarkers (Year 2) | Mean arterial pressure (mmHg) | 64.44 (60.78, 68.78) |
|  |  | Resting heart rate (bpm) | 109 (99.33, 118.67) |
|  | Glucocorticoid receptor percent methylation | NR3C1 exon 1F promoter | -5.66 (-6.06, -5.32) |
|  |  | NGFI-A transcription factor binding site | -4.48 (-4.65, -4.14) |
|  | Child development (Year 1) | WHO Gross Motor Milestone sum score | 2 (1, 4) |
|  |  | CDI expressive language z-score | 0.02 (-0.54, 0.74) |
|  |  | CDI language understanding z-score | 0.09 (-0.56, 0.78) |
|  | Child development (Year 2) | EASQ communication z-score | 0.37 (-0.39, 0.75) |
|  |  | EASQ motor development z-score | -0.15 (-0.59, 0.87) |
|  |  | EASQ personal-social development z-score | 0.14 (-0.49, 1) |
|  |  | EASQ combined z-score | 0.3 (-0.37, 0.86) |
|  |  | CDI expressive language z-score | 0.27 (-0.57, 0.8) |
|  |  | CDI language understanding z-score | 0.12 (-0.48, 0.74) |
|  | Anthropometry (14 months, Year 1) | Length-for-age Z score | -1.42 (-2.07, -0.76) |
|  |  | Weight-for-age Z score | -1.31 (-2.01, -0.64) |
|  |  | Weight-for-length Z score | -0.9 (-1.56, -0.23) |
|  |  | Head circumference-for-age Z score | -1.79 (-2.35, -1.13) |
|  | Anthropometry (28 months, Year 2) | Length-for-age Z score | -1.56 (-2.28, -0.95) |
|  |  | Weight-for-age Z score | -1.58 (-2.2, -0.94) |
|  |  | Weight-for-length Z score | -1.03 (-1.62, -0.38) |
|  |  | Head circumference-for-age Z score | -1.81 (-2.38, -1.21) |
|  | Diarrhea (14 months, Year 1) | Caregiver-reported 7-day recall | 195 (13%) |
|  | Diarrhea (28 months, Year 2) | Caregiver-reported 7-day recall | 110 (7%) |
| Mother |  | Age (years) | 24 (20, 27) |
|  | Anthropometry at enrollment | Height (cm) | 150.2 (146.8, 154.05) |
|  | Education | Schooling completed (years) | 7 (4, 9) |
|  | Depression at Year 1 | CES-D score | 10 (6, 16) |
|  | Depression at Year 2 | CES-D score | 10 (5, 17) |
|  | Perceived stress at Year 2 | Perceived Stress Scale score | 14 (10, 17.25) |
|  | Intimate partner violence | Any lifetime exposure | 810 (57%) |

## Table 2. Salivary stress biomarkers and child development at Year 2

| Exposure | Outcome | N | 25th Percentile | 75th Percentile | Outcome, 75th Percentile v. 25th Percentile | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  | Unadjusted | | | | Adjusted | | | |
|  |  |  |  |  | Predicted Outcome at 25th Percentile | Predicted Outcome at 75th Percentile | Coefficient (95% CI) | P-value | Predicted Outcome at 25th Percentile | Predicted Outcome at 75th Percentile | Coefficient (95% CI) | P-value |
| Cortisol Reactivity (ug/dl/min) | EASQ Communication Score | 649 | 0 | 0.01 | 0.11 | 0.14 | 0.03 (-0.06, 0.12) | 0.5 | 0.23 | 0.25 | 0.02 (-0.07, 0.11) | 0.67 |
|  | EASQ Gross Motor Score | 646 | 0 | 0.01 | 0.09 | 0.08 | -0.01 (-0.11, 0.1) | 0.91 | -0.09 | -0.11 | -0.01 (-0.13, 0.1) | 0.81 |
|  | EASQ Personal Social Score | 649 | 0 | 0.01 | 0.15 | 0.17 | 0.02 (-0.07, 0.12) | 0.64 | 0.57 | 0.43 | -0.14 (-0.4, 0.12) | 0.3 |
|  | Combined EASQ | 647 | 0 | 0.01 | 0.12 | 0.14 | 0.01 (-0.08, 0.11) | 0.77 | 0.13 | 0.13 | -0.01 (-0.1, 0.09) | 0.9 |
|  | CDI expressive language Z-score | 658 | 0 | 0.01 | 0.15 | 0.01 | -0.14 (-0.31, 0.04) | 0.14 | -0.01 | -0.24 | -0.23 (-0.45, 0) | 0.05 |
|  | CDI comprehension Z-score | 655 | 0 | 0.01 | 0.02 | -0.02 | -0.04 (-0.13, 0.05) | 0.4 | -0.01 | -0.16 | -0.15 (-0.29, -0.01) | 0.04 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pre-stressor Cortisol (ug/dl) | EASQ Communication Score | 708 | -2.51 | -1.66 | 0.12 | 0.08 | -0.04 (-0.13, 0.05) | 0.42 | 0.32 | 0.24 | -0.07 (-0.32, 0.17) | 0.57 |
|  | EASQ Gross Motor Score | 706 | -2.51 | -1.66 | 0.13 | 0.09 | -0.05 (-0.14, 0.05) | 0.35 | 0.24 | 0.17 | -0.07 (-0.21, 0.07) | 0.31 |
|  | EASQ Personal Social Score | 709 | -2.51 | -1.66 | 0.13 | 0.08 | -0.04 (-0.24, 0.16) | 0.69 | 0.57 | 0.47 | -0.1 (-0.33, 0.12) | 0.38 |
|  | Combined EASQ | 707 | -2.51 | -1.66 | 0.11 | 0.08 | -0.04 (-0.13, 0.06) | 0.47 | 0.27 | 0.09 | -0.17 (-0.38, 0.03) | 0.1 |
|  | CDI expressive language Z-score | 717 | -2.51 | -1.66 | 0.12 | 0.1 | -0.02 (-0.1, 0.07) | 0.7 | -0.06 | -0.11 | -0.04 (-0.13, 0.05) | 0.35 |
|  | CDI comprehension Z-score | 715 | -2.51 | -1.66 | 0.02 | 0 | -0.02 (-0.11, 0.07) | 0.66 | 0.02 | -0.03 | -0.05 (-0.14, 0.04) | 0.28 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| Post-stressor Cortisol (ug/dl) | EASQ Communication Score | 655 | -2.06 | -0.6 | 0.12 | 0.12 | 0.01 (-0.1, 0.12) | 0.88 | 0.34 | 0.19 | -0.16 (-0.32, 0.01) | 0.06 |
|  | EASQ Gross Motor Score | 651 | -2.06 | -0.6 | 0.11 | 0.07 | -0.04 (-0.15, 0.07) | 0.48 | 0.12 | 0.07 | -0.05 (-0.17, 0.07) | 0.42 |
|  | EASQ Personal Social Score | 655 | -2.06 | -0.6 | 0.16 | 0.17 | 0.01 (-0.11, 0.13) | 0.85 | 0.46 | 0.43 | -0.04 (-0.16, 0.09) | 0.59 |
|  | Combined EASQ | 653 | -2.06 | -0.6 | 0.19 | 0.11 | -0.08 (-0.23, 0.07) | 0.29 | 0.29 | 0.07 | -0.22 (-0.41, -0.04) | 0.02 |
|  | CDI expressive language Z-score | 664 | -2.06 | -0.6 | 0.14 | 0.08 | -0.06 (-0.17, 0.05) | 0.29 | -0.09 | -0.16 | -0.07 (-0.18, 0.04) | 0.24 |
|  | CDI comprehension Z-score | 661 | -2.06 | -0.59 | 0.04 | -0.04 | -0.08 (-0.19, 0.03) | 0.18 | 0.01 | -0.12 | -0.12 (-0.24, -0.01) | 0.04 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| sAA Reactivity (U/ml/min) | EASQ Communication Score | 660 | -0.05 | 4.52 | 0.06 | 0.1 | 0.03 (-0.02, 0.09) | 0.26 | 0.11 | 0.13 | 0.02 (-0.04, 0.07) | 0.57 |
|  | EASQ Gross Motor Score | 657 | -0.04 | 4.5 | 0.07 | 0.13 | 0.07 (0, 0.14) | 0.06 | -0.08 | -0.05 | 0.04 (-0.03, 0.1) | 0.26 |
|  | EASQ Personal Social Score | 660 | -0.05 | 4.52 | 0.08 | 0.13 | 0.05 (-0.01, 0.11) | 0.09 | 0.32 | 0.37 | 0.06 (-0.18, 0.3) | 0.65 |
|  | Combined EASQ | 658 | -0.06 | 4.5 | -0.01 | 0.15 | 0.16 (-0.04, 0.36) | 0.11 | 0.03 | 0.18 | 0.15 (-0.06, 0.36) | 0.16 |
|  | CDI expressive language Z-score | 668 | -0.07 | 4.48 | 0.11 | 0.11 | 0 (0, 0) | 1 | -0.2 | -0.18 | 0.02 (-0.03, 0.08) | 0.45 |
|  | CDI comprehension Z-score | 665 | -0.04 | 4.49 | -0.03 | 0.02 | 0.05 (0, 0.11) | 0.06 | -0.05 | -0.02 | 0.03 (-0.03, 0.09) | 0.29 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| Pre-stressor sAA (U/ml) | EASQ Communication Score | 703 | 3.49 | 4.64 | 0.13 | 0.05 | -0.08 (-0.18, 0.01) | 0.08 | 0.25 | 0.17 | -0.09 (-0.18, 0.01) | 0.07 |
|  | EASQ Gross Motor Score | 701 | 3.49 | 4.64 | 0.2 | 0.06 | -0.14 (-0.31, 0.03) | 0.1 | 0.04 | -0.14 | -0.18 (-0.35, 0) | 0.04 |
|  | EASQ Personal Social Score | 704 | 3.49 | 4.64 | 0.15 | 0.12 | -0.04 (-0.14, 0.07) | 0.5 | 0.45 | 0.43 | -0.02 (-0.23, 0.19) | 0.84 |
|  | Combined EASQ | 702 | 3.49 | 4.64 | 0.21 | 0.04 | -0.16 (-0.36, 0.03) | 0.1 | 0.23 | 0.04 | -0.19 (-0.4, 0.02) | 0.07 |
|  | CDI expressive language Z-score | 712 | 3.49 | 4.64 | 0.1 | 0.06 | -0.04 (-0.17, 0.09) | 0.58 | -0.1 | -0.16 | -0.07 (-0.22, 0.08) | 0.39 |
|  | CDI comprehension Z-score | 710 | 3.49 | 4.64 | 0 | -0.03 | -0.02 (-0.15, 0.1) | 0.72 | 0.05 | 0.01 | -0.04 (-0.15, 0.06) | 0.42 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| Post-stressor sAA (U/ml) | EASQ Communication Score | 672 | 3.9 | 5.15 | 0.1 | 0.11 | 0.01 (-0.08, 0.1) | 0.83 | 0.22 | 0.22 | 0 (-0.1, 0.09) | 0.98 |
|  | EASQ Gross Motor Score | 668 | 3.9 | 5.15 | 0.1 | 0.12 | 0.02 (-0.08, 0.11) | 0.76 | 0.21 | 0.19 | -0.02 (-0.12, 0.09) | 0.78 |
|  | EASQ Personal Social Score | 672 | 3.9 | 5.15 | 0.11 | 0.17 | 0.06 (-0.05, 0.17) | 0.28 | 0.45 | 0.47 | 0.02 (-0.08, 0.13) | 0.66 |
|  | Combined EASQ | 670 | 3.9 | 5.15 | 0.11 | 0.14 | 0.03 (-0.06, 0.13) | 0.51 | 0.18 | 0.19 | 0.01 (-0.09, 0.11) | 0.9 |
|  | CDI expressive language Z-score | 680 | 3.9 | 5.15 | 0.08 | 0.14 | 0.06 (-0.05, 0.17) | 0.31 | -0.19 | -0.16 | 0.03 (-0.06, 0.13) | 0.53 |
|  | CDI comprehension Z-score | 677 | 3.9 | 5.15 | -0.02 | 0.04 | 0.06 (-0.05, 0.17) | 0.29 | -0.08 | -0.04 | 0.04 (-0.05, 0.14) | 0.37 |
| N, 25th Percentile, and 75th Percentile are from the unadjusted analyses | | | | | | | | | | | | |

## Table 3. Glucocortoid receptor methylation and child development at Year 2

| Exposure | Outcome | N | 25th Percentile | 75th Percentile | Outcome, 75th Percentile v. 25th Percentile | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  | Unadjusted | | | | Adjusted | | | |
|  |  |  |  |  | Predicted Outcome at 25th Percentile | Predicted Outcome at 75th Percentile | Coefficient (95% CI) | P-value | Predicted Outcome at 25th Percentile | Predicted Outcome at 75th Percentile | Coefficient (95% CI) | P-value |
| Mean Overall Percentage Glucocorticoid Receptor Methylation | EASQ Communication Score | 665 | -6.06 | -5.32 | 0.12 | 0.11 | -0.02 (-0.09, 0.06) | 0.69 | 0.25 | 0.22 | -0.02 (-0.1, 0.06) | 0.58 |
|  | EASQ Gross Motor Score | 662 | -6.06 | -5.32 | 0.11 | 0.11 | 0 (-0.08, 0.08) | 0.97 | -0.06 | -0.05 | 0.01 (-0.08, 0.1) | 0.82 |
|  | EASQ Personal Social Score | 666 | -6.06 | -5.32 | 0.18 | 0.14 | -0.05 (-0.13, 0.04) | 0.3 | 0.44 | 0.36 | -0.08 (-0.17, 0.01) | 0.07 |
|  | Combined EASQ | 664 | -6.06 | -5.32 | 0.08 | 0.1 | 0.02 (-0.19, 0.24) | 0.85 | 0.12 | 0.13 | 0.01 (-0.21, 0.23) | 0.95 |
|  | CDI expressive language Z-score | 673 | -6.06 | -5.32 | 0.16 | 0.07 | -0.09 (-0.17, -0.01) | 0.02 | 0.18 | 0.09 | -0.09 (-0.17, -0.01) | 0.03 |
|  | CDI comprehension Z-score | 671 | -6.06 | -5.32 | 0.08 | -0.03 | -0.11 (-0.19, -0.02) | 0.01 | 0.1 | 0.01 | -0.09 (-0.19, 0.01) | 0.07 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| Percentage methylation at NGFI-A transcription factor binding site (CpG site #12) | EASQ Communication Score | 399 | -4.65 | -4.15 | 0.08 | 0.09 | 0.01 (-0.09, 0.11) | 0.85 | 0.04 | 0.02 | -0.02 (-0.13, 0.09) | 0.71 |
|  | EASQ Gross Motor Score | 397 | -4.64 | -4.14 | 0.03 | 0.15 | 0.12 (0, 0.23) | 0.04 | 0.02 | 0.2 | 0.18 (0, 0.37) | 0.05 |
|  | EASQ Personal Social Score | 400 | -4.65 | -4.15 | 0.1 | 0.15 | 0.04 (-0.07, 0.16) | 0.48 | 0.35 | 0.36 | 0.01 (-0.11, 0.13) | 0.9 |
|  | Combined EASQ | 398 | -4.64 | -4.15 | 0.09 | 0.14 | 0.05 (-0.06, 0.17) | 0.39 | 0 | 0.03 | 0.03 (-0.08, 0.14) | 0.62 |
|  | CDI expressive language Z-score | 404 | -4.65 | -4.14 | 0.2 | 0.17 | -0.03 (-0.14, 0.08) | 0.58 | 0.32 | 0.29 | -0.03 (-0.14, 0.08) | 0.63 |
|  | CDI comprehension Z-score | 403 | -4.65 | -4.14 | 0.09 | 0.07 | -0.02 (-0.13, 0.1) | 0.79 | -0.13 | -0.2 | -0.07 (-0.18, 0.05) | 0.26 |
| N, 25th Percentile, and 75th Percentile are from the unadjusted analyses | | | | | | | | | | | | |

## Table 4. Urinary isoprostanes and child development at Year 1

| Exposure | Outcome | N | 25th Percentile | 75th Percentile | Outcome, 75th Percentile v. 25th Percentile | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  | Unadjusted | | | | Adjusted | | | |
|  |  |  |  |  | Predicted Outcome at 25th Percentile | Predicted Outcome at 75th Percentile | Coefficient (95% CI) | P-value | Predicted Outcome at 25th Percentile | Predicted Outcome at 75th Percentile | Coefficient (95% CI) | P-value |
| IPF(2a)-III (ng/mg creatinine) | Sum of 2nd, 4th, 5th, and 6th WHO motor milestones | 674 | -0.72 | -0.1 | 2.4 | 2.43 | 0.04 (-0.31, 0.38) | 0.84 | 1.84 | 1.79 | -0.05 (-0.37, 0.27) | 0.77 |
|  | CDI expressive language Z-score | 675 | -0.72 | -0.1 | 0.23 | 0.26 | 0.03 (-0.13, 0.18) | 0.76 | 0.26 | 0.31 | 0.05 (-0.1, 0.2) | 0.52 |
|  | CDI comprehension Z-score | 679 | -0.72 | -0.09 | 0.37 | 0.4 | 0.02 (-0.07, 0.11) | 0.61 | 0.37 | 0.43 | 0.06 (-0.04, 0.16) | 0.24 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| 2,3-dinor-iPF(2a)-III (ng/mg creatinine) | Sum of 2nd, 4th, 5th, and 6th WHO motor milestones | 674 | 1.55 | 1.97 | 2.28 | 2.63 | 0.35 (0.02, 0.68) | 0.04 | 1.81 | 2.09 | 0.27 (0.04, 0.51) | 0.02 |
|  | CDI expressive language Z-score | 675 | 1.55 | 1.97 | 0.25 | 0.21 | -0.04 (-0.13, 0.06) | 0.43 | 0.25 | 0.27 | 0.01 (-0.09, 0.11) | 0.8 |
|  | CDI comprehension Z-score | 679 | 1.55 | 1.97 | 0.41 | 0.32 | -0.09 (-0.19, 0.01) | 0.08 | 0.35 | 0.36 | 0.01 (-0.11, 0.12) | 0.89 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| iPF(2a)-VI (ng/mg creatinine) | Sum of 2nd, 4th, 5th, and 6th WHO motor milestones | 674 | 2.31 | 2.87 | 2.4 | 2.58 | 0.18 (-0.04, 0.41) | 0.11 | 1.92 | 1.92 | 0 (-0.15, 0.15) | 0.98 |
|  | CDI expressive language Z-score | 675 | 2.31 | 2.87 | 0.25 | 0.21 | -0.05 (-0.14, 0.05) | 0.33 | 0.2 | 0.22 | 0.02 (-0.2, 0.24) | 0.86 |
|  | CDI comprehension Z-score | 679 | 2.31 | 2.87 | 0.39 | 0.36 | -0.03 (-0.13, 0.07) | 0.59 | 0.38 | 0.43 | 0.05 (-0.08, 0.18) | 0.43 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| 8,12-iso-iPF(2a)-VI (ng/mg creatinine) | Sum of 2nd, 4th, 5th, and 6th WHO motor milestones | 674 | 2.16 | 2.92 | 2.44 | 2.54 | 0.09 (-0.11, 0.29) | 0.37 | 1.9 | 1.91 | 0.01 (-0.17, 0.19) | 0.94 |
|  | CDI expressive language Z-score | 675 | 2.17 | 2.92 | 0.13 | 0.33 | 0.2 (-0.01, 0.42) | 0.06 | 0.19 | 0.36 | 0.17 (-0.03, 0.38) | 0.09 |
|  | CDI comprehension Z-score | 679 | 2.17 | 2.92 | 0.27 | 0.49 | 0.22 (-0.02, 0.45) | 0.07 | 0.29 | 0.44 | 0.15 (0.04, 0.27) | 0.01 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| Combined urinary oxidative stress biomarker score | Sum of 2nd, 4th, 5th, and 6th WHO motor milestones | 674 | 2.48 | 3.54 | 2.37 | 2.6 | 0.24 (0, 0.48) | 0.05 | 1.88 | 1.96 | 0.09 (-0.11, 0.29) | 0.41 |
|  | CDI expressive language Z-score | 675 | 2.49 | 3.54 | 0.05 | 0.26 | 0.2 (-0.04, 0.45) | 0.1 | 0.1 | 0.31 | 0.21 (-0.03, 0.44) | 0.08 |
|  | CDI comprehension Z-score | 679 | 2.49 | 3.54 | 0.37 | 0.4 | 0.03 (-0.08, 0.14) | 0.61 | 0.22 | 0.4 | 0.18 (-0.08, 0.44) | 0.18 |
| N, 25th Percentile, and 75th Percentile are from the unadjusted analyses | | | | | | | | | | | | |

## Table 5. Urinary isoprostanes at Year 1 and child development at Year 2

| Exposure | Outcome | N | 25th Percentile | 75th Percentile | Outcome, 75th Percentile v. 25th Percentile | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  | Unadjusted | | | | Adjusted | | | |
|  |  |  |  |  | Predicted Outcome at 25th Percentile | Predicted Outcome at 75th Percentile | Coefficient (95% CI) | P-value | Predicted Outcome at 25th Percentile | Predicted Outcome at 75th Percentile | Coefficient (95% CI) | P-value |
| IPF(2a)-III (ng/mg creatinine) | EASQ Communication Score | 620 | -0.73 | -0.09 | 0.11 | 0.09 | -0.02 (-0.1, 0.07) | 0.74 | 0.19 | 0.21 | 0.01 (-0.07, 0.1) | 0.79 |
|  | EASQ Gross Motor Score | 619 | -0.73 | -0.09 | 0.18 | 0.08 | -0.09 (-0.18, -0.01) | 0.04 | 0.32 | 0.24 | -0.08 (-0.18, 0.01) | 0.08 |
|  | EASQ Personal Social Score | 621 | -0.73 | -0.09 | 0.15 | 0.11 | -0.04 (-0.15, 0.07) | 0.47 | 0.42 | 0.41 | 0 (-0.12, 0.11) | 0.97 |
|  | Combined EASQ Score | 619 | -0.73 | -0.09 | 0.13 | 0.09 | -0.04 (-0.13, 0.05) | 0.36 | 0.23 | 0.21 | -0.01 (-0.1, 0.08) | 0.8 |
|  | CDI expressive language Z-score | 629 | -0.73 | -0.09 | 0.05 | 0.14 | 0.08 (-0.08, 0.25) | 0.31 | 0 | 0.05 | 0.04 (-0.04, 0.13) | 0.34 |
|  | CDI comprehension Z-score | 627 | -0.73 | -0.09 | 0 | 0.02 | 0.03 (-0.06, 0.11) | 0.56 | 0.07 | 0.13 | 0.06 (-0.03, 0.15) | 0.21 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| 2,3-dinor-iPF(2a)-III (ng/mg creatinine) | EASQ Communication Score | 620 | 1.54 | 1.96 | 0.15 | 0.06 | -0.09 (-0.2, 0.02) | 0.11 | 0.21 | 0.17 | -0.04 (-0.15, 0.07) | 0.49 |
|  | EASQ Gross Motor Score | 619 | 1.54 | 1.96 | 0.15 | 0.09 | -0.06 (-0.31, 0.18) | 0.62 | 0.37 | 0.29 | -0.08 (-0.34, 0.18) | 0.55 |
|  | EASQ Personal Social Score | 621 | 1.54 | 1.96 | 0.19 | 0.01 | -0.18 (-0.43, 0.08) | 0.18 | 0.42 | 0.35 | -0.07 (-0.22, 0.08) | 0.38 |
|  | Combined EASQ Score | 619 | 1.54 | 1.96 | 0.18 | 0 | -0.18 (-0.43, 0.07) | 0.15 | 0.21 | 0.12 | -0.09 (-0.22, 0.05) | 0.21 |
|  | CDI expressive language Z-score | 629 | 1.52 | 1.96 | 0.16 | 0.12 | -0.04 (-0.19, 0.1) | 0.56 | 0.01 | -0.03 | -0.04 (-0.18, 0.1) | 0.6 |
|  | CDI comprehension Z-score | 627 | 1.54 | 1.96 | 0.04 | -0.05 | -0.09 (-0.21, 0.03) | 0.13 | 0.08 | 0.05 | -0.03 (-0.15, 0.09) | 0.64 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| iPF(2a)-VI (ng/mg creatinine) | EASQ Communication Score | 620 | 2.31 | 2.87 | 0.15 | 0.02 | -0.13 (-0.22, -0.03) | 0.01 | 0.18 | 0.1 | -0.08 (-0.21, 0.04) | 0.19 |
|  | EASQ Gross Motor Score | 619 | 2.31 | 2.87 | 0.13 | 0.13 | 0 (0, 0) | 1 | 0.33 | 0.27 | -0.07 (-0.17, 0.04) | 0.22 |
|  | EASQ Personal Social Score | 621 | 2.31 | 2.87 | 0.16 | -0.01 | -0.17 (-0.27, -0.07) | 0 | 0.42 | 0.28 | -0.14 (-0.25, -0.03) | 0.01 |
|  | Combined EASQ Score | 619 | 2.31 | 2.87 | 0.15 | 0 | -0.15 (-0.24, -0.05) | 0 | 0.22 | 0.12 | -0.1 (-0.23, 0.04) | 0.15 |
|  | CDI expressive language Z-score | 629 | 2.3 | 2.87 | 0.1 | 0.1 | 0 (0, 0) | 1 | 0.01 | -0.07 | -0.08 (-0.17, 0.02) | 0.12 |
|  | CDI comprehension Z-score | 627 | 2.31 | 2.87 | 0.02 | -0.04 | -0.07 (-0.16, 0.03) | 0.17 | 0.06 | 0.05 | -0.01 (-0.15, 0.13) | 0.91 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| 8,12-iso-iPF(2a)-VI (ng/mg creatinine) | EASQ Communication Score | 620 | 2.14 | 2.92 | 0.08 | 0.12 | 0.04 (-0.07, 0.15) | 0.48 | 0.2 | 0.26 | 0.06 (-0.07, 0.19) | 0.36 |
|  | EASQ Gross Motor Score | 619 | 2.14 | 2.92 | 0.14 | 0.13 | -0.01 (-0.11, 0.1) | 0.89 | 0.29 | 0.31 | 0.02 (-0.09, 0.13) | 0.76 |
|  | EASQ Personal Social Score | 621 | 2.15 | 2.92 | 0.14 | 0.11 | -0.03 (-0.14, 0.09) | 0.66 | 0.41 | 0.42 | 0 (-0.12, 0.12) | 0.97 |
|  | Combined EASQ Score | 619 | 2.14 | 2.92 | 0.11 | 0.13 | 0.02 (-0.09, 0.14) | 0.73 | 0.21 | 0.25 | 0.04 (-0.1, 0.17) | 0.6 |
|  | CDI expressive language Z-score | 629 | 2.15 | 2.92 | 0.07 | 0.13 | 0.06 (-0.04, 0.16) | 0.24 | 0.01 | -0.02 | -0.03 (-0.22, 0.16) | 0.76 |
|  | CDI comprehension Z-score | 627 | 2.15 | 2.92 | -0.09 | 0.1 | 0.19 (-0.03, 0.41) | 0.09 | 0.03 | 0.09 | 0.05 (-0.13, 0.24) | 0.57 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| Combined urinary oxidative stress biomarker score | EASQ Communication Score | 620 | 2.47 | 3.56 | 0.12 | 0.08 | -0.04 (-0.14, 0.07) | 0.49 | 0.19 | 0.19 | -0.01 (-0.11, 0.1) | 0.9 |
|  | EASQ Gross Motor Score | 619 | 2.47 | 3.56 | 0.17 | 0.1 | -0.07 (-0.18, 0.03) | 0.17 | 0.32 | 0.27 | -0.06 (-0.17, 0.05) | 0.31 |
|  | EASQ Personal Social Score | 621 | 2.47 | 3.56 | 0.15 | 0.06 | -0.09 (-0.21, 0.02) | 0.11 | 0.42 | 0.38 | -0.04 (-0.16, 0.08) | 0.49 |
|  | Combined EASQ Score | 619 | 2.47 | 3.56 | 0.13 | 0.06 | -0.07 (-0.18, 0.04) | 0.21 | 0.23 | 0.19 | -0.04 (-0.15, 0.08) | 0.54 |
|  | CDI expressive language Z-score | 629 | 2.46 | 3.55 | 0.09 | 0.11 | 0.02 (-0.08, 0.13) | 0.65 | 0 | 0.02 | 0.02 (-0.08, 0.12) | 0.72 |
|  | CDI comprehension Z-score | 627 | 2.46 | 3.55 | 0 | 0.01 | 0.01 (-0.09, 0.12) | 0.83 | 0.05 | 0.11 | 0.06 (-0.05, 0.17) | 0.28 |
| N, 25th Percentile, and 75th Percentile are from the unadjusted analyses | | | | | | | | | | | | |

## Table 6. Urinary isoprostanes and time to WHO motor milestone at Year 1

| Exposure | Outcome | N | 25th Percentile | 75th Percentile | Outcome, 75th Percentile v. 25th Percentile | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  | Unadjusted | | Adjusted | |
|  |  |  |  |  | Hazard Ratio (95% CI) | P-value | Hazard Ratio (95% CI) | P-value |
| IPF(2a)-III (ng/mg creatinine) | Time to sitting unsupported | 683 | -0.72 | -0.09 | 1 (0.8, 1.24) | 0.97 | 0 (0, 727975445160237568) | 0.61 |
|  | Time to crawling | 682 | -0.72 | -0.09 | 1.05 (0.95, 1.17) | 0.35 | 1.02 (0.91, 1.14) | 0.76 |
|  | Time to standing with support | 678 | -0.73 | -0.1 | 0.88 (0.63, 1.24) | 0.48 | 1.01 (0.88, 1.17) | 0.86 |
|  | Time to walking with support | 677 | -0.72 | -0.1 | 0.99 (0.72, 1.37) | 0.97 | 1.03 (0.9, 1.17) | 0.72 |
|  | Time to standing unsupported | 679 | -0.72 | -0.09 | 1.11 (0.79, 1.55) | 0.56 | 0.95 (0.65, 1.39) | 0.79 |
|  | Time to walking unsupported | 679 | -0.72 | -0.09 | 1.14 (0.97, 1.35) | 0.11 | 1.05 (0.88, 1.25) | 0.6 |
|  |  |  |  |  |  |  |  |  |
| 2,3-dinor-iPF(2a)-III (ng/mg creatinine) | Time to sitting unsupported | 683 | 1.55 | 1.97 | 1.04 (0.81, 1.32) | 0.78 | 0 (0, 1.18552134902425e+59) | 0.76 |
|  | Time to crawling | 682 | 1.55 | 1.97 | 1.09 (0.8, 1.48) | 0.62 | 1 (0.72, 1.37) | 0.98 |
|  | Time to standing with support | 678 | 1.55 | 1.97 | 0.97 (0.84, 1.11) | 0.64 | 0.95 (0.81, 1.11) | 0.55 |
|  | Time to walking with support | 677 | 1.55 | 1.97 | 1.02 (0.88, 1.19) | 0.77 | 0.97 (0.82, 1.15) | 0.72 |
|  | Time to standing unsupported | 679 | 1.55 | 1.97 | 1.45 (1, 2.11) | 0.05 | 1.12 (0.93, 1.33) | 0.23 |
|  | Time to walking unsupported | 679 | 1.55 | 1.97 | 1.46 (0.93, 2.29) | 0.1 | 1 (0.81, 1.23) | 1 |
|  |  |  |  |  |  |  |  |  |
| iPF(2a)-VI (ng/mg creatinine) | Time to sitting unsupported | 683 | 2.31 | 2.87 | 2.05 (0.23, 18.13) | 0.53 | 624959704.4 (0, 8.78286913170087e+65) | 0.78 |
|  | Time to crawling | 682 | 2.31 | 2.87 | 1.03 (0.92, 1.16) | 0.64 | 1 (0.89, 1.14) | 0.97 |
|  | Time to standing with support | 678 | 2.31 | 2.87 | 0.94 (0.84, 1.06) | 0.34 | 0.91 (0.78, 1.06) | 0.22 |
|  | Time to walking with support | 677 | 2.31 | 2.87 | 1.24 (1, 1.54) | 0.05 | 1.12 (0.88, 1.42) | 0.35 |
|  | Time to standing unsupported | 679 | 2.31 | 2.87 | 1.21 (0.92, 1.58) | 0.17 | 0.8 (0.51, 1.26) | 0.35 |
|  | Time to walking unsupported | 679 | 2.31 | 2.87 | 1.24 (0.94, 1.64) | 0.13 | 1.02 (0.76, 1.37) | 0.88 |
|  |  |  |  |  |  |  |  |  |
| 8,12-iso-iPF(2a)-VI (ng/mg creatinine) | Time to sitting unsupported | 683 | 2.17 | 2.91 | 0.94 (0.5, 1.77) | 0.87 | 0.03 (0, 2645605214851898) | 0.87 |
|  | Time to crawling | 682 | 2.17 | 2.92 | 1.02 (0.9, 1.16) | 0.75 | 0.98 (0.86, 1.12) | 0.79 |
|  | Time to standing with support | 678 | 2.16 | 2.91 | 0.93 (0.82, 1.06) | 0.31 | 0.88 (0.74, 1.04) | 0.12 |
|  | Time to walking with support | 677 | 2.16 | 2.91 | 1.02 (0.85, 1.23) | 0.81 | 0.99 (0.8, 1.23) | 0.95 |
|  | Time to standing unsupported | 679 | 2.16 | 2.91 | 1.14 (0.89, 1.47) | 0.3 | 1.07 (0.79, 1.45) | 0.69 |
|  | Time to walking unsupported | 679 | 2.17 | 2.91 | 1.17 (0.97, 1.42) | 0.1 | 1.12 (0.81, 1.53) | 0.51 |
|  |  |  |  |  |  |  |  |  |
| Combined urinary oxidative stress biomarker score | Time to sitting unsupported | 683 | 2.49 | 3.54 | 0.7 (0.15, 3.33) | 0.67 | 0 (0, 520427180630980) | 0.52 |
|  | Time to crawling | 682 | 2.49 | 3.54 | 1.04 (0.91, 1.18) | 0.58 | 0.99 (0.87, 1.14) | 0.93 |
|  | Time to standing with support | 678 | 2.48 | 3.54 | 1.11 (0.78, 1.58) | 0.59 | 1.12 (0.75, 1.69) | 0.59 |
|  | Time to walking with support | 677 | 2.48 | 3.54 | 1.06 (0.9, 1.26) | 0.48 | 1 (0.84, 1.2) | 0.98 |
|  | Time to standing unsupported | 679 | 2.48 | 3.54 | 1.39 (0.96, 2.01) | 0.08 | 1.2 (0.8, 1.82) | 0.38 |
|  | Time to walking unsupported | 679 | 2.49 | 3.54 | 1.61 (1.12, 2.33) | 0.01 | 0.98 (0.79, 1.22) | 0.87 |
| N, 25th Percentile, and 75th Percentile are from the unadjusted analyses | | | | | | | | |
| Hazard ratio could not be estimated for sitting without support since nearly all children had achieved this milestone before time of measurement | | | | | | | | |

## Table 7. Mean arterial pressure and heart rate and child development at Year 2

| Exposure | Outcome | N | 25th Percentile | 75th Percentile | Outcome, 75th Percentile v. 25th Percentile | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  | Unadjusted | | | | Adjusted | | | |
|  |  |  |  |  | Predicted Outcome at 25th Percentile | Predicted Outcome at 75th Percentile | Coefficient (95% CI) | P-value | Predicted Outcome at 25th Percentile | Predicted Outcome at 75th Percentile | Coefficient (95% CI) | P-value |
| Mean arterial pressure (mmHg) | EASQ Communication Score | 1421 | 60.78 | 68.78 | 0.07 | 0.16 | 0.09 (-0.05, 0.23) | 0.21 | -0.18 | -0.13 | 0.04 (-0.04, 0.12) | 0.29 |
|  | EASQ Gross Motor Score | 1413 | 60.78 | 68.78 | 0.11 | 0.15 | 0.04 (-0.02, 0.1) | 0.2 | 0.38 | 0.4 | 0.02 (-0.04, 0.09) | 0.49 |
|  | EASQ Personal Social Score | 1421 | 60.78 | 68.78 | 0.2 | 0.16 | -0.04 (-0.21, 0.13) | 0.67 | 0.04 | -0.04 | -0.08 (-0.26, 0.09) | 0.35 |
|  | Combined EASQ | 1416 | 60.78 | 68.78 | 0.13 | 0.2 | 0.07 (-0.09, 0.22) | 0.39 | 0.07 | 0.09 | 0.02 (-0.14, 0.17) | 0.85 |
|  | CDI expressive language Z-score | 1438 | 60.81 | 68.78 | 0.04 | 0.12 | 0.08 (-0.08, 0.24) | 0.31 | -0.02 | 0.07 | 0.09 (-0.08, 0.25) | 0.31 |
|  | CDI comprehension Z-score | 1433 | 60.78 | 68.78 | 0.01 | 0.04 | 0.02 (-0.13, 0.18) | 0.76 | 0.02 | 0.01 | -0.01 (-0.16, 0.15) | 0.92 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| Mean Resting Heart Rate (bpm) | EASQ Communication Score | 1424 | 99.33 | 118.67 | 0.1 | 0.06 | -0.04 (-0.13, 0.04) | 0.35 | -0.15 | -0.15 | -0.01 (-0.07, 0.06) | 0.89 |
|  | EASQ Gross Motor Score | 1415 | 99.33 | 118.67 | 0.18 | 0.09 | -0.08 (-0.19, 0.02) | 0.1 | 0.39 | 0.37 | -0.02 (-0.08, 0.05) | 0.58 |
|  | EASQ Personal Social Score | 1424 | 99.33 | 118.67 | 0.25 | 0.1 | -0.15 (-0.31, 0) | 0.06 | 0.03 | -0.07 | -0.1 (-0.25, 0.06) | 0.23 |
|  | Combined EASQ | 1418 | 99.33 | 118.67 | 0.18 | 0.09 | -0.08 (-0.2, 0.03) | 0.17 | -0.09 | -0.11 | -0.02 (-0.1, 0.06) | 0.68 |
|  | CDI expressive language Z-score | 1441 | 99.67 | 118.67 | 0.15 | 0.03 | -0.11 (-0.22, -0.01) | 0.03 | 0.01 | -0.03 | -0.04 (-0.11, 0.02) | 0.18 |
|  | CDI comprehension Z-score | 1434 | 99.33 | 118.67 | 0.13 | -0.07 | -0.19 (-0.35, -0.04) | 0.01 | -0.01 | -0.04 | -0.03 (-0.09, 0.03) | 0.27 |
| N, 25th Percentile, and 75th Percentile are from the unadjusted analyses | | | | | | | | | | | | |