Table S1. Pearson correlation coefficients of log10-transformed SG adjusted for estrogen concentrations during the first, second and third trimesters of pregnancy

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Estrogens** | | **1st trimester** | | | **2nd trimester** | | | **3rd trimester** | | | |
| **E1** | **E2** | **E3** | **E1** | **E2** | **E3** | **E1** | **E2** | **E3** |
| **1st trimester** | E1 | 1.00 |  |  |  |  |  |  |  |  |
| E2 | 0.83\*\* | 1.00 |  |  |  |  |  |  |  |
| E3 | 0.33\*\* | 0.42\*\* | 1.00 |  |  |  |  |  |  |
| **2nd trimester** | E1 | 0.52\*\* | 0.39\*\* | 0.09\*\* | 1.00 |  |  |  |  |  |
| E2 | 0.41\*\* | 0.43\*\* | 0.09\*\* | 0.85\*\* | 1.00 |  |  |  |  |
| E3 | 0.12\*\* | 0.13\*\* | 0.26\*\* | 0.49\*\* | 0.54\*\* | 1.00 |  |  |  |
| **3rd trimester** | E1 | 0.50\*\* | 0.38\*\* | 0.16\*\* | 0.51\*\* | 0.37\*\* | 0.15\*\* | 1.00 |  |  |
| E2 | 0.37\*\* | 0.40\*\* | 0.17\*\* | 0.36\*\* | 0.41\*\* | 0.16\*\* | 0.82\*\* | 1.00 |  |
| E3 | 0.09\* | 0.10\*\* | 0.38\*\* | 0.19\*\* | 0.18\*\* | 0.39\*\* | 0.43\*\* | 0.51\*\* | 1.00 |

E1, estrone; E2, estradiol; E3, estriol; SG, specific gravity.

\**p* < 0.05, \*\**p* < 0.01.

Table S2. Regression coefficients [β (95% CI)] for trimester-specific associations of maternal estrogen concentrations with fetal sizes at 16 and 31 weeks

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Fetal size (z-scores)** | **Estrogens in the 1st trimester** | | | **Estrogens in the 2nd trimester** | | |
| **E1** | **E2** | **E3** | **E1** | **E2** | **E3** |
| **At 16 weeks (n = 680)** |  |  |  |  |  |  |
| FL | 0.08 (-0.15, 0.30) | 0.12 (-0.12, 0.36) | 0.31 (0.12, 0.50)\*\* | / | / | / |
| BPD | -0.02 (-0.22, 0.18) | 0.02 (-0.20, 0.24) | 0.21 (0.04, 0.38)\* | / | / | / |
| AC | 0.14 (-0.08, 0.36) | 0.24 (0.001, 0.49)\* | 0.27 (0.08, 0.47)\*\* | / | / | / |
| HC | -0.12 (-0.34, 0.09) | -0.02 (-0.26, 0.22) | 0.21 (0.02, 0.40)\* | / | / | / |
| EFW | 0.10 (-0.12, 0.32) | 0.19 (-0.05, 0.43) | 0.32 (0.13, 0.51)\*\* | / | / | / |
| **At 31 weeks (n = 769)** |  |  |  |  |  |  |
| FL | -0.02 (-0.22, 0.18) | 0.09 (-0.14, 0.31) | 0.25 (0.08, 0.42)\*\* | 0.15 (-0.03, 0.33) | 0.16 (-0.04, 0.37) | 0.25 (0.09, 0.42)\*\* |
| BPD | 0.14 (-0.05, 0.32) | 0.09 (-0.12, 0.30) | 0.08 (-0.07, 0.24) | 0.08 (-0.08, 0.24) | 0.004 (-0.18, 0.19) | 0.11 (-0.04, 0.27) |
| AC | 0.15 (-0.04, 0.35) | 0.07 (-0.14, 0.29) | 0.15 (-0.01 , 0.32) | 0.05 (-0.12, 0.22) | -0.02 (-0.22, 0.17) | 0.08 (-0.08, 0.24) |
| HC | 0.08 (-0.10, 0.27) | 0.08 (-0.13, 0.29) | 0.08 (-0.08, 0.23) | 0.09 (-0.07, 0.26) | 0.02 (-0.17, 0.21) | 0.19 (0.03, 0.34)\* |
| EFW | 0.12 (-0.07, 0.31) | 0.11 (-0.11, 0.33) | 0.21 (0.05, 0.38)\*\* | 0.11 (-0.06, 0.28) | 0.05 (-0.15, 0.25) | 0.19 (0.03, 0.35)\* |

E1, estrone; E2, estradiol; E3, estriol; FL, femur length; BPD, biparietal diameter; AC, abdominal circumference; HC, head circumference; EFW, estimated fetal weight; CI, confidence interval.

Adjusted for maternal age, parity, education level, pre-pregnancy body mass index, passive smoking during pregnancy, maternal height, paternal height, infant gender, season of birth, gestational week of urine collection.

*\*p* < 0.05, *\*\*p* < 0.01.

Table S3. Regression coefficients [β (95% CI)] of multivariable linear regression model for age-specific associations of maternal estrogen concentrations with weight and height z-scores from birth to 24 months of age

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Neonatal and childhood**  **anthropometry** | **Estrogens in the 1st trimester** | | | **Estrogens in the 2nd trimester** | | | **Estrogens in the 3rd trimester** | | | |
| **E1** | **E2** | **E3** | **E1** | **E2** | **E3** | **E1** | **E2** | **E3** |
| **Weight z-scores a** |  |  |  |  |  |  |  |  |  |
| At birth (n = 852) c | 0.08 (-0.08, 0.24) | 0.05 (-0.13, 0.23) | 0.12 (-0.01, 0.26) | 0.15 (0.01, 0.30)\* | 0.16 (-0.01, 0.32) | 0.22 (0.08, 0.35)\*\* | 0.17 (0.02, 0.33)\* | 0.20 (0.04, 0.36)\* | 0.23 (0.11, 0.36)\*\* |
| 6 months (n = 758) | 0.05 (-0.12, 0.22) | 0.10 (-0.09, 0.29) | 0.10 (-0.04, 0.24) | 0.03 (-0.12, 0.18) | 0.01 (-0.17, 0.18) | 0.03 (-0.12, 0.17) | 0.03 (-0.13, 0.20) | 0.03 (-0.15, 0.20) | -0.02 (-0.16, 0.11) |
| 12 months (n = 792) | 0.06 (-0.09, 0.22) | 0.04 (-0.14, 0.22) | 0.06 (-0.08, 0.19) | -0.01 (-0.15, 0.14) | -0.06 (-0.22, 0.11) | 0.004 (-0.13, 0.14) | 0.05 (-0.10, 0.21) | 0.05 (-0.11, 0.21) | 0.02 (-0.10, 0.15) |
| 24 months (n = 610) | 0.09 (-0.09, 0.27) | 0.08 (-0.12, 0.29) | 0.14 (-0.01, 0.29) | 0.12 (-0.04, 0.28) | 0.07 (-0.12, 0.25) | 0.14 (-0.01, 0.28) | 0.16 (-0.02, 0.34) | 0.15 (-0.04, 0.34) | 0.07 (-0.07, 0.21) |
| **Height z-scores b** |  |  |  |  |  |  |  |  |  |
| At birth (n = 852) c | 0.03 (-0.12, 0.18) | 0.04 (-0.13, 0.20) | 0.14 (0.02, 0.27)\* | 0.06 (-0.07, 0.20) | 0.08 (-0.07, 0.24) | 0.14 (0.02, 0.27)\* | 0.11 (-0.04, 0.25) | 0.17 (0.02, 0.32)\* | 0.18 (0.07, 0.30)\*\* |
| 6 months (n = 758) | 0.08 (-0.09, 0.25) | 0.14 (-0.06, 0.33) | 0.18 (0.03, 0.32)\* | 0.16 (0.005, 0.32)\* | 0.17 (-0.01, 0.35) | 0.21 (0.06, 0.35)\*\* | -0.08 (-0.26, 0.09) | -0.13 (-0.31, 0.05) | -0.08 (-0.22, 0.05) |
| 12 months (n = 785) | 0.08 (-0.10, 0.25) | 0.09 (-0.10, 0.29) | 0.14 (-0.01, 0.29) | 0.003 (-0.16, 0.16) | -0.002 (-0.18, 0.18) | 0.12 (-0.02, 0.27) | -0.08 (-0.25, 0.09) | -0.12 (-0.30, 0.05) | -0.02 (-0.15, 0.12) |
| 24 months (n = 609) | 0.15 (-0.04, 0.35) | 0.17 (-0.05, 0.38) | 0.11 (-0.06, 0.27) | 0.18 (0.01, 0.36)\* | 0.12 (-0.07, 0.32) | 0.19 (0.04, 0.35)\* | 0.17 (-0.03, 0.36) | 0.15 (-0.06, 0.36) | 0.03 (-0.12, 0.18) |

E1, estrone; E2, estradiol; E3, estriol; CI, confidence interval.

a Adjusted for maternal age, parity, education level, passive smoking during pregnancy, pre-pregnancy body mass index, infant gender, season of birth, pregnancy weight gain, gestational week of urine collection, birth weight.

b Adjusted for maternal age, parity, education level, passive smoking during pregnancy, pre-pregnancy body mass index, maternal height, paternal height, infant gender, season of birth, gestational week of urine collection, birth length.

c Adjusted as Model a and b expect for birth weight or birth length.

*\*p* < 0.05, *\*\*p* < 0.01.

Table S4.Regression coefficients [β (95% CI)] of linear mixed models for associations of maternal estrogen concentrations with weight and height z-scores from birth to 24 months of age (n = 852)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Estrogens** | | **Weight z-score a** | ***p*-int** | **Height z-score b** | ***p*-int** |
| E1 | 1st trimester | 0.08 (-0.08, 0.25) | 0.96 | 0.04 (-0.12, 0.21) | 0.71 |
| 2nd trimester | 0.13 (-0.02, 0.28) | 0.71 | 0.05 (-0.10, 0.20) | 0.10 |
| 3rd trimester | 0.17 (0.01, 0.33)\* | 0.69 | 0.10 (-0.06, 0.26) | 0.10 |
| E2 | 1st trimester | 0.06 (-0.12, 0.24) | 0.96 | 0.05 (-0.13, 0.24) | 0.73 |
| 2nd trimester | 0.14 (-0.03, 0.31) | 0.59 | 0.08 (-0.10, 0.25) | 0.30 |
| 3rd trimester | 0.21 (0.04, 0.37)\* | 0.66 | 0.17 (-0.01, 0.34) | 0.01 |
| E3 | 1st trimester | 0.13 (-0.01, 0.26) | 0.84 | 0.16 (0.02, 0.30)\* | 0.72 |
| 2nd trimester | 0.21 (0.07, 0.35)\*\* | 0.39 | 0.14 (0.004, 0.28)\* | 0.41 |
| 3rd trimester | 0.24 (0.11, 0.37)\*\* | 0.04 | 0.21 (0.08, 0.34)\*\* | 0.005 |

E1, estrone; E2, estradiol; E3, estriol; CI, confidence interval.

a Adjusted for maternal age, parity, education level, passive smoking during pregnancy, pre-pregnancy body mass index, infant age, infant gender, season of birth, pregnancy weight gain, gestational week of urine collection.

b Adjusted for maternal age, parity, education level, passive smoking during pregnancy, pre-pregnancy body mass index, infant age, maternal height, paternal height, infant gender, season of birth, gestational week of urine collection.

*p*-int represent the P value of interaction term between infant age and log10-transformed SG adjusted urinary estrogen concentrations.

\**p* < 0.05, \*\**p* < 0.01.

Table S5. Sensitivity analyses of age-specific associations between maternal estrogen concentrations and weight and height z-scores from birth to 24 months of age

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Neonatal and childhood**  **anthropometry** | **Estrogens in the 1st trimester** | | | **Estrogens in the 2nd trimester** | | | | **Estrogens in the 3rd trimester** | | |
| **E1** | **E2** | **E3** | | **E1** | **E2** | **E3** | **E1** | **E2** | **E3** |
| **Weight z-scores a** |  |  |  | |  |  |  |  |  |  |
| At birth (n = 776) c | 0.06 (-0.07, 0.19) | -0.004 (-0.15, 0.15) | 0.10 (-0.02, 0.22) | | 0.12 (-0.01, 0.24) | 0.11 (-0.03, 0.25) | 0.21 (0.10, 0.33)\*\* | 0.14 (0.01, 0.27)\* | 0.16 (0.02, 0.29)\* | 0.20 (0.09, 0.31)\*\* |
| 6 months (n = 694) | 0.03 (-0.15, 0.20) | 0.08 (-0.11, 0.28) | 0.11 (-0.04, 0.26) | | 0.01 (-0.15, 0.17) | 0.01 (-0.17, 0.19) | -0.003 (-0.16, 0.15) | 0.03 (-0.15, 0.20) | 0.02 (-0.17, 0.20) | -0.05 (-0.20, 0.09) |
| 12 months (n = 724) | 0.05 (-0.11, 0.21) | 0.04 (-0.14, 0.23) | 0.06 (-0.08, 0.21) | | -0.01 (-0.16, 0.14) | -0.05 (-0.22, 0.12) | -0.04 (-0.19, 0.11) | 0.08 (-0.08, 0.24) | 0.08 (-0.09, 0.25) | 0.04 (-0.10, 0.17) |
| 24 months (n = 557) | 0.03 (-0.16, 0.22) | 0.04 (-0.17, 0.24) | 0.15 (-0.02, 0.31) | | 0.10 (-0.07, 0.26) | 0.05 (-0.14, 0.24) | 0.10 (-0.06, 0.26) | 0.15 (-0.03, 0.34) | 0.14 (-0.05, 0.34) | 0.07 (-0.08, 0.22) |
| **Height z-scores b** |  |  |  | |  |  |  |  |  |  |
| At birth (n = 776) c | 0.01 (-0.12, 0.14) | -0.01 (-0.16, 0.13) | 0.11 (-0.01, 0.22) | | 0.005 (-0.11, 0.12) | 0.01 (-0.12, 0.15) | 0.11 (-0.003, 0.23) | 0.03 (-0.10, 0.16) | 0.10 (-0.03, 0.23) | 0.14 (0.04, 0.25)\* |
| 6 months (n = 694) | 0.05 (-0.13, 0.23) | 0.11 (-0.09, 0.31) | 0.18 (0.02, 0.34)\* | | 0.15 (-0.01, 0.32) | 0.17 (-0.01, 0.36) | 0.18 (0.02, 0.34)\* | -0.09 (-0.27, 0.09) | -0.14 (-0.33, 0.05) | -0.12 (-0.26, 0.03) |
| 12 months (n = 724) | 0.08 (-0.11, 0.26) | 0.11 (-0.09, 0.32) | 0.15 (-0.01, 0.31) | | 0.03 (-0.14, 0.19) | 0.02 (-0.17, 0.20) | 0.10 (-0.06, 0.26) | -0.03 (-0.20, 0.15) | -0.07 (-0.26, 0.11) | 0.04 (-0.11, 0.19) |
| 24 months (n = 557) | 0.12 (-0.09, 0.32) | 0.15 (-0.08, 0.37) | 0.18 (-0.001, 0.35) | | 0.19 (0.01, 0.36)\* | 0.13 (-0.07, 0.33) | 0.17 (0.001, 0.34)\* | 0.21 (0.01, 0.41)\* | 0.19 (-0.02, 0.41) | 0.08 (-0.08, 0.25) |

E1, estrone; E2, estradiol; E3, estriol; CI, confidence interval.

a Adjusted for maternal age, parity, education level, passive smoking during pregnancy, pre-pregnancy body mass index, infant gender, season of birth, pregnancy weight gain, gestational week of urine collection, birth weight.

b Adjusted for maternal age, parity, education level, passive smoking during pregnancy, pre-pregnancy body mass index, maternal height, paternal height, infant gender, season of birth, gestational week of urine collection, birth length.

c Adjusted as Model a and b expect for birth weight or birth length.

\**p* < 0.05, \*\**p* < 0.01.