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Supplemental Material

Critical Windows for Associations between Manganese Exposure during Pregnancy and Size at Birth: A Longitudinal Cohort Study in Wuhan, China

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Table of Contents

Table S1. The distributions of urinary concentrations of Mn and other toxic metals.

Table S2. Characteristics of parents and children (term births) in the study population (Wuhan, China).

Table S3. Correlation coefficients for urinary Mn concentrations and urinary concentrations of other toxic metals.

Table S4. Associations of SG-adjusted urinary Mn concentrations ($\mu\text{g/L}$) during pregnancy with size at birth.

Table S5. Associations of SG-adjusted urinary Mn concentrations ($\mu\text{g/L}$) during pregnancy with size at birth among term births.

Table S6. Adjusted associations of SG-adjusted urinary Mn concentrations ($\mu\text{g/L}$) during pregnancy with size at birth among women without pregnancy complications.

Table S7. Adjusted associations of SG-adjusted urinary Mn concentrations ($\mu\text{g/L}$) during pregnancy with size at birth among women who provided completed three urine samples.

Table S8. Adjusted associations of overall quintiles for SG-adjusted urinary Mn concentrations ($\mu\text{g/L}$) during pregnancy with size at birth.

Table S9. Adjusted associations of unadjusted urinary Mn concentrations ($\mu\text{g/L}$) during pregnancy with size at birth.

Table S10. Adjusted associations of SG-adjusted urinary Mn concentrations ($\mu\text{g/L}$) during pregnancy with size at birth, stratified by infant sex and maternal age at recruitment.

Figure S1. Relative exposure of Mn comparing newborns in the 10th percentile of birth weight, birth length, or Ponderal index with those in the 90th percentile among term births. Solid lines represent relative exposures of Mn through the whole pregnancy, comparing newborns in the 10th percentiles of A) birth weight, B) birth length, or C) Ponderal index to those in the 90th percentiles. Dotted lines represent pointwise 95% confidence intervals. Models were adjusted for gestational age at delivery, maternal age at recruitment, parity, pre-pregnancy BMI, alcohol consumption before pregnancy, active smoking before pregnancy, passive smoking during pregnancy, education, folic acid supplementation, physical activity during pregnancy, and infant sex. The model for birth length model was additionally adjusted for maternal and paternal height.

Figure S2. Relative exposure of Mn comparing newborns in the 10th percentile of birth weight, birth length, or Ponderal index with those in the 90th percentile among women who provided completed three urine samples. Solid lines represent relative exposures of Mn through the whole pregnancy, comparing newborns in the 10th percentiles of A) birth weight, B) birth length, or C) Ponderal index to those in the 90th percentiles. Dotted lines represent pointwise 95% confidence intervals. Models were adjusted for gestational age at delivery, maternal age at recruitment, parity, pre-pregnancy BMI, alcohol consumption before pregnancy, active smoking before pregnancy, passive smoking during pregnancy, education, folic acid supplementation, physical activity during pregnancy, and infant sex. The model for birth length model was additionally adjusted for maternal and paternal height.

Table S1. The distributions of urinary concentrations of Mn and other toxic metals.

| | No. | Arithmetic mean (95% CI) | Geometric mean (95% CI) | Selected percentiles | | | | | No. (%) < LOQ | LOQ | Spike- recovery | Measurement variations | | |
|---------------------------|------|-----------------------------|----------------------------|----------------------|------------------|------------------|------------------|------------------|------------------|-----|--------------------|------------------------|-----------|-------|
| | | | | 5 th | 25 th | 50 th | 75 th | 95 th | | | | Intra-day | Inter-day | |
| Manganese | | | | | | | | | | | 0.150 | 106.44% | 0.29% | 0.27% |
| Unadjusted | | | | | | | | | | | | | | |
| All measures | 6078 | 2.40 (2.25, 2.56) | 1.39 (1.36, 1.42) | 0.31 | 0.78 | 1.37 | 2.48 | 6.32 | 134 (2.20%) | | | | | |
| 1 st trimester | 2771 | 2.55 (2.28, 2.83) | 1.44 (1.39, 1.49) | 0.33 | 0.80 | 1.45 | 2.57 | 6.19 | 52 (1.88%) | | | | | |
| 2 nd trimester | 1481 | 2.01 (1.84, 2.18) | 1.21 (1.15, 1.27) | 0.27 | 0.72 | 1.16 | 2.03 | 5.18 | 36 (2.43%) | | | | | |
| 3 rd trimester | 1826 | 2.50 (2.25, 2.74) | 1.47 (1.41, 1.54) | 0.31 | 0.82 | 1.47 | 2.69 | 7.17 | 46 (2.52%) | | | | | |
| SG-adjusted | | | | | | | | | | | | | | |
| All measures | 6078 | 3.09 (2.88, 3.30) | 1.46 (1.42, 1.50) | 0.27 | 0.72 | 1.41 | 2.78 | 10.1 | 128 (2.11%) | | | | | |
| 1 st trimester | 2771 | 2.89 (2.63, 3.15) | 1.38 (1.33, 1.44) | 0.26 | 0.68 | 1.35 | 2.65 | 9.89 | 61 (2.20%) | | | | | |
| 2 nd trimester | 1481 | 2.72 (2.43, 3.00) | 1.38 (1.30, 1.45) | 0.28 | 0.70 | 1.29 | 2.57 | 8.24 | 29 (1.96%) | | | | | |
| 3 rd trimester | 1826 | 3.69 (3.15, 4.24) | 1.66 (1.58, 1.75) | 0.28 | 0.83 | 1.63 | 3.08 | 11.5 | 38 (2.08%) | | | | | |
| Vanadium | | | | | | | | | | | 0.008 | 105.13% | 0.55% | 0.44% |
| Unadjusted | | | | | | | | | | | | | | |
| All measures | 6078 | 0.97 (0.95, 1.00) | 0.80 (0.78, 0.81) | 0.26 | 0.54 | 0.85 | 1.21 | 2.13 | 2 (0.03%) | | | | | |
| 1 st trimester | 2771 | 1.04 (1.01, 1.06) | 0.85 (0.83, 0.87) | 0.25 | 0.59 | 0.93 | 1.32 | 2.26 | 2 (0.07%) | | | | | |
| 2 nd trimester | 1481 | 0.84 (0.82, 0.86) | 0.72 (0.70, 0.74) | 0.27 | 0.49 | 0.77 | 1.08 | 1.71 | 0 (0.00%) | | | | | |
| 3 rd trimester | 1826 | 0.99 (0.94, 1.04) | 0.78 (0.76, 0.81) | 0.28 | 0.53 | 0.81 | 1.16 | 2.16 | 0 (0.00%) | | | | | |
| SG-adjusted | | | | | | | | | | | | | | |
| All measures | 6078 | 1.01 (0.99, 1.03) | 0.84 (0.83, 0.85) | 0.32 | 0.60 | 0.83 | 1.18 | 2.24 | 1 (0.02%) | | | | | |
| 1 st trimester | 2771 | 0.98 (0.95, 1.00) | 0.82 (0.80, 0.83) | 0.29 | 0.60 | 0.82 | 1.15 | 2.15 | 1 (0.04%) | | | | | |
| 2 nd trimester | 1481 | 0.95 (0.92, 0.98) | 0.82 (0.80, 0.85) | 0.35 | 0.59 | 0.82 | 1.12 | 1.90 | 0 (0.00%) | | | | | |
| 3 rd trimester | 1826 | 1.10 (1.06, 1.14) | 0.89 (0.86, 0.91) | 0.33 | 0.60 | 0.87 | 1.28 | 2.66 | 0 (0.00%) | | | | | |
| Arsenic | | | | | | | | | | | 0.060 | 99.52% | 0.68% | 0.28% |
| Unadjusted | | | | | | | | | | | | | | |
| All measures | 6078 | 28.0 (26.4, 29.6) | 17.2 (16.8, 17.6) | 3.6 | 9.3 | 17.3 | 31.7 | 80.5 | 2 (0.03%) | | | | | |
| 1 st trimester | 2771 | 32.5 (29.5, 35.6) | 19.5 (18.8, 20.2) | 3.8 | 10.6 | 20.2 | 36.1 | 90.0 | 2 (0.07%) | | | | | |
| 2 nd trimester | 1481 | 22.7 (21.2, 24.2) | 14.9 (14.2, 15.6) | 3.5 | 8.1 | 14.7 | 26.3 | 67.6 | 0 (0.00%) | | | | | |
| 3 rd trimester | 1826 | 25.5 (23.3, 27.6) | 15.9 (15.2, 16.6) | 3.5 | 8.7 | 15.9 | 29.3 | 72.5 | 0 (0.00%) | | | | | |

| | | | | | | | | | | |
|---------------------------|------|-------------------|-------------------|------|------|------|------|------|----|---------|
| SG-adjusted | | | | | | | | | | |
| All measures | 6078 | 24.1 (23.2, 25.0) | 18.1 (17.7, 18.4) | 7.0 | 11.7 | 16.9 | 26.6 | 60.5 | 2 | (0.03%) |
| 1 st trimester | 2771 | 25.6 (24.0, 27.3) | 18.7 (18.2, 19.3) | 7.4 | 12.1 | 17.5 | 27.7 | 63.8 | 2 | (0.07%) |
| 2 nd trimester | 1481 | 21.7 (20.6, 22.8) | 17.0 (16.4, 17.5) | 7.0 | 11.1 | 15.5 | 24.3 | 55.7 | 0 | (0.00%) |
| 3 rd trimester | 1826 | 23.8 (22.3, 25.2) | 18.0 (17.4, 18.5) | 6.4 | 11.7 | 17.3 | 26.6 | 60.4 | 0 | (0.00%) |
| Cadmium | | | | | | | | | | |
| | | | | | | | | | | |
| Unadjusted | | | | | | | | | | |
| All measures | 6078 | 0.67 (0.65, 0.69) | 0.46 (0.44, 0.47) | 0.11 | 0.25 | 0.47 | 0.83 | 1.96 | 8 | (0.13%) |
| 1 st trimester | 2771 | 0.84 (0.81, 0.87) | 0.56 (0.54, 0.58) | 0.12 | 0.31 | 0.60 | 1.08 | 2.37 | 5 | (0.18%) |
| 2 nd trimester | 1481 | 0.53 (0.50, 0.55) | 0.38 (0.37, 0.40) | 0.10 | 0.23 | 0.39 | 0.65 | 1.33 | 1 | (0.07%) |
| 3 rd trimester | 1826 | 0.54 (0.52, 0.57) | 0.38 (0.37, 0.40) | 0.10 | 0.22 | 0.39 | 0.67 | 1.52 | 2 | (0.11%) |
| SG-adjusted | | | | | | | | | | |
| All measures | 6078 | 0.62 (0.60, 0.63) | 0.48 (0.47, 0.49) | 0.17 | 0.31 | 0.47 | 0.74 | 1.55 | 4 | (0.07%) |
| 1 st trimester | 2771 | 0.70 (0.68, 0.72) | 0.54 (0.52, 0.55) | 0.18 | 0.35 | 0.53 | 0.85 | 1.78 | 3 | (0.11%) |
| 2 nd trimester | 1481 | 0.53 (0.51, 0.55) | 0.43 (0.42, 0.45) | 0.17 | 0.29 | 0.42 | 0.64 | 1.18 | 0 | (0.00%) |
| 3 rd trimester | 1826 | 0.56 (0.54, 0.59) | 0.43 (0.42, 0.45) | 0.15 | 0.28 | 0.42 | 0.67 | 1.37 | 1 | (0.05%) |
| Lead | | | | | | | | | | |
| | | | | | | | | | | |
| Unadjusted | | | | | | | | | | |
| All measures | 6078 | 3.55 (3.31, 3.78) | 2.32 (2.27, 2.37) | 0.63 | 1.43 | 2.34 | 3.90 | 9.26 | 43 | (0.71%) |
| 1 st trimester | 2771 | 4.06 (3.75, 4.36) | 2.72 (2.62, 2.81) | 0.72 | 1.66 | 2.81 | 4.70 | 10.6 | 18 | (0.65%) |
| 2 nd trimester | 1481 | 3.21 (2.45, 3.96) | 1.94 (1.86, 2.03) | 0.59 | 1.26 | 1.93 | 2.98 | 7.36 | 9 | (0.61%) |
| 3 rd trimester | 1826 | 3.05 (2.89, 3.22) | 2.11 (2.02, 2.20) | 0.56 | 1.34 | 2.17 | 3.55 | 8.41 | 16 | (0.88%) |
| SG-adjusted | | | | | | | | | | |
| All measures | 6078 | 3.88 (3.58, 4.18) | 2.44 (2.39, 2.49) | 0.83 | 1.50 | 2.27 | 3.82 | 10.3 | 23 | (0.38%) |
| 1 st trimester | 2771 | 3.92 (3.67, 4.17) | 2.61 (2.53, 2.70) | 0.87 | 1.60 | 2.42 | 4.22 | 10.6 | 7 | (0.25%) |
| 2 nd trimester | 1481 | 3.96 (2.88, 5.05) | 2.21 (2.12, 2.31) | 0.83 | 1.41 | 2.02 | 3.18 | 8.59 | 6 | (0.41%) |
| 3 rd trimester | 1826 | 3.75 (3.49, 4.01) | 2.38 (2.28, 2.49) | 0.71 | 1.47 | 2.28 | 3.85 | 11.5 | 10 | (0.55%) |

0.003 98.81% 0.89% 0.36%

0.023 100.12% 0.78% 0.98%

Abbreviations: No., number; CI, confidence interval; LOQ, limit of quantification; SG, specific gravity.

Table S2. Characteristics of parents and children (term births) in the study population (Wuhan, China).

| Term births | No. (%) or Mean \pm SD |
|---|--------------------------|
| | 2923 |
| Maternal characteristics | |
| Age at recruitment, years | 27.85 \pm 3.40 |
| < 25 | 380 (13.00) |
| 25 - 30 | 1773 (60.66) |
| 30 - 35 | 639 (21.86) |
| \geq 35 | 131 (4.48) |
| Pre-pregnancy BMI, kg/m² | 20.86 \pm 2.82 |
| < 18.5 | 552 (18.88) |
| 18.5 - 23.9 | 2000 (68.42) |
| 24.0 - 27.9 | 309 (10.57) |
| \geq 28.0 | 62 (2.12) |
| Height, m | 1.61 \pm 0.05 |
| Parity | |
| Nulliparous | 2495 (85.36) |
| Multiparous | 428 (14.64) |
| Anemia during pregnancy | |
| No | 2810 (96.13) |
| Yes | 113 (3.87) |
| Hypertensive disorders of pregnancy | |
| No | 2836 (97.02) |
| Hypertension | 60 (2.05) |
| Pre-eclampsia | 27 (0.92) |
| Gestational diabetes mellitus | |
| No | 2674 (91.48) |
| Yes | 249 (8.52) |
| Active smoking before pregnancy | |
| No | 2905 (99.38) |
| Yes | 18 (0.62) |
| Passive smoking during pregnancy | |
| No | 2074 (70.95) |
| Yes | 849 (29.05) |
| Alcohol consumption before pregnancy | |
| No | 2898 (99.14) |
| Yes | 25 (0.86) |
| Education | |
| Compulsory and lower (\leq 9 years) | 183 (6.26) |
| High school and equal (9 - 12 years) | 435 (14.88) |
| Graduate and higher ($>$ 12 years) | 2305 (78.86) |
| Folic acid supplementation | |
| No | 481 (16.46) |
| Only in the 1 st trimester | 1010 (34.55) |
| Only in the 2 nd and 3 rd trimester | 602 (20.60) |
| During the entire pregnancy | 830 (28.40) |
| Physical activity during pregnancy | |

| | |
|---|-------------------------|
| No | 264 (9.03) |
| 1 - 4 day/week | 461 (15.77) |
| 5 - 7 day/week | 2198 (75.20) |
| Paternal height, m | 1.74 ± 0.05 |
| Neonatal characteristics | |
| Infant sex | |
| Male infant | 1542 (52.75) |
| Female infant | 1381 (47.25) |
| Gestational age, week | 39.41 ± 0.98 |
| Birth weight, g | 3350.61 ± 405.93 |
| Birth length, cm | 50.37 ± 1.51 |
| Ponderal index, kg/m³ | 26.14 ± 2.06 |

Abbreviations: No., number; SD, standard deviation; BMI, body mass index.

Table S3. Correlation coefficients for urinary Mn concentrations and urinary concentrations of other toxic metals.

| | | Manganese | Vanadium | Arsenic | Cadmium | Lead |
|---------------------------------|----------|------------------|-----------------|----------------|----------------|-------------|
| 1st trimester | | | | | | |
| Manganese | r | 1.000 | 0.551 | 0.136 | 0.236 | 0.565 |
| | P | | < 0.0001 | < 0.0001 | < 0.0001 | < 0.0001 |
| Vanadium | r | | 1.000 | 0.275 | 0.407 | 0.517 |
| | P | | | < 0.0001 | < 0.0001 | < 0.0001 |
| Arsenic | r | | | 1.000 | 0.474 | 0.330 |
| | P | | | | < 0.0001 | < 0.0001 |
| Cadmium | r | | | | 1.000 | 0.389 |
| | P | | | | | < 0.0001 |
| Lead | r | | | | | 1.000 |
| 2nd trimester | | | | | | |
| Manganese | r | 1.000 | 0.542 | 0.073 | 0.203 | 0.529 |
| | P | | < 0.0001 | 0.0049 | < 0.0001 | < 0.0001 |
| Vanadium | r | | 1.000 | 0.033 | 0.273 | 0.439 |
| | P | | | 0.2015 | < 0.0001 | < 0.0001 |
| Arsenic | r | | | 1.000 | 0.325 | 0.189 |
| | P | | | | < 0.0001 | < 0.0001 |
| Cadmium | r | | | | 1.000 | 0.299 |
| | P | | | | | < 0.0001 |
| Lead | r | | | | | 1.000 |
| 3rd trimester | | | | | | |
| Manganese | r | 1.000 | 0.555 | 0.147 | 0.325 | 0.556 |
| | P | | < 0.0001 | < 0.0001 | < 0.0001 | < 0.0001 |
| Vanadium | r | | 1.000 | 0.228 | 0.387 | 0.489 |
| | P | | | < 0.0001 | < 0.0001 | < 0.0001 |
| Arsenic | r | | | 1.000 | 0.483 | 0.295 |
| | P | | | | < 0.0001 | < 0.0001 |
| Cadmium | r | | | | 1.000 | 0.384 |
| | P | | | | | < 0.0001 |
| Lead | r | | | | | 1.000 |

Table S4. Associations of SG-adjusted urinary Mn concentrations ($\mu\text{g/L}$) during pregnancy with size at birth.

| | β (95% CI) for quintiles of urinary manganese concentrations ($\mu\text{g/L}$) | | | |
|---|--|----------------------|----------------------|----------------------|
| | Model 1 | Model 2 | Model 3 | Model 4 |
| Birth weight, g | | | | |
| 1st trimester | | | | |
| < 0.57 | 15.9 (-29.6, 61.5) | -1.2 (-45.3, 43.0) | 1.6 (-42.3, 45.4) | -5.8 (-51.4, 39.7) |
| 0.57 - 1.05 | -4.2 (-27.4, 19.0) | -7.9 (-30.1, 14.4) | -6.2 (-28.4, 16.0) | -8.9 (-31.3, 13.6) |
| 1.05 - 1.72 | Reference | Reference | Reference | Reference |
| 1.72 - 3.13 | -1.3 (-12.6, 10.0) | -3.3 (-14.3, 7.6) | -2.8 (-13.7, 8.1) | -3.6 (-14.6, 7.4) |
| ≥ 3.13 | -3.2 (-12.3, 5.9) | -3.0 (-11.8, 5.8) | -2.8 (-11.6, 5.9) | -2.6 (-12.0, 6.9) |
| 2nd trimester | | | | |
| < 0.61 | -5.5 (-69.1, 58.1) | -13.2 (-73.4, 47.0) | -12.2 (-72.4, 48.0) | -12.8 (-74.1, 48.6) |
| 0.61 - 1.02 | -22.6 (-53.9, 8.6) | -20.2 (-50.5, 10.0) | -20.1 (-50.3, 10.1) | -20.6 (-50.8, 9.5) |
| 1.02 - 1.63 | Reference | Reference | Reference | Reference |
| 1.63 - 3.15 | -6.5 (-22.2, 9.2) | -4.0 (-19.1, 11.1) | -3.7 (-18.8, 11.3) | -4.7 (-20.0, 10.6) |
| ≥ 3.15 | -15.6 (-28.1, -3.1) | -13.0 (-25.2, -0.9) | -12.6 (-24.7, -0.4) | -13.9 (-27.5, -0.4) |
| 3rd trimester | | | | |
| < 0.69 | -2.5 (-60.9, 55.9) | -0.6 (-57.1, 55.9) | -1.6 (-58.0, 54.8) | -3.2 (-61.8, 55.5) |
| 0.69 - 1.26 | -29.8 (-57.9, -1.8) | -23.6 (-50.9, 3.8) | -22.6 (-49.8, 4.7) | -24.2 (-52.0, 3.6) |
| 1.26 - 2.12 | Reference | Reference | Reference | Reference |
| 2.12 - 3.89 | -26.5 (-40.6, -12.4) | -21.2 (-35.0, -7.5) | -21.3 (-35.0, -7.6) | -21.2 (-35.0, -7.4) |
| ≥ 3.89 | -15.6 (-27.0, -4.2) | -11.2 (-22.2, -0.1) | -11.2 (-22.2, -0.2) | -10.9 (-22.8, 1.0) |
| Birth length, cm | | | | |
| 1st trimester | | | | |
| < 0.57 | -0.05 (-0.22, 0.13) | -0.08 (-0.25, 0.09) | -0.07 (-0.24, 0.09) | -0.09 (-0.26, 0.08) |
| 0.57 - 1.05 | -0.02 (-0.10, 0.07) | -0.03 (-0.11, 0.05) | -0.02 (-0.10, 0.06) | -0.03 (-0.11, 0.06) |
| 1.05 - 1.72 | Reference | Reference | Reference | Reference |
| 1.72 - 3.13 | -0.02 (-0.06, 0.02) | -0.02 (-0.06, 0.02) | -0.02 (-0.06, 0.02) | -0.02 (-0.06, 0.02) |
| ≥ 3.13 | -0.02 (-0.05, 0.02) | -0.01 (-0.05, 0.02) | -0.01 (-0.05, 0.02) | -0.01 (-0.05, 0.02) |
| 2nd trimester | | | | |
| < 0.61 | -0.03 (-0.28, 0.22) | -0.10 (-0.33, 0.13) | -0.10 (-0.34, 0.13) | -0.09 (-0.33, 0.15) |
| 0.61 - 1.02 | -0.05 (-0.17, 0.07) | -0.04 (-0.15, 0.07) | -0.04 (-0.16, 0.07) | -0.03 (-0.15, 0.08) |
| 1.02 - 1.63 | Reference | Reference | Reference | Reference |
| 1.63 - 3.15 | -0.02 (-0.08, 0.04) | -0.01 (-0.06, 0.05) | -0.01 (-0.06, 0.05) | -0.01 (-0.07, 0.05) |
| ≥ 3.15 | -0.02 (-0.06, 0.03) | -0.01 (-0.06, 0.03) | -0.01 (-0.06, 0.03) | -0.02 (-0.07, 0.03) |
| 3rd trimester | | | | |
| < 0.69 | -0.04 (-0.25, 0.18) | -0.05 (-0.25, 0.15) | -0.06 (-0.26, 0.15) | -0.05 (-0.26, 0.16) |
| 0.69 - 1.26 | -0.10 (-0.21, 0.00) | -0.07 (-0.17, 0.03) | -0.07 (-0.17, 0.03) | -0.08 (-0.18, 0.02) |
| 1.26 - 2.12 | Reference | Reference | Reference | Reference |
| 2.12 - 3.89 | -0.10 (-0.15, -0.05) | -0.08 (-0.13, -0.03) | -0.08 (-0.13, -0.03) | -0.08 (-0.13, -0.03) |
| ≥ 3.89 | -0.06 (-0.10, -0.02) | -0.04 (-0.08, 0.00) | -0.04 (-0.08, 0.00) | -0.04 (-0.08, 0.00) |
| Ponderal index, kg/m^3 | | | | |
| 1st trimester | | | | |
| < 0.57 | 0.23 (-0.01, 0.47) | 0.18 (-0.06, 0.42) | 0.19 (-0.05, 0.42) | 0.15 (-0.10, 0.39) |
| 0.57 - 1.05 | 0.00 (-0.12, 0.12) | -0.02 (-0.13, 0.10) | -0.01 (-0.13, 0.11) | -0.03 (-0.14, 0.09) |
| 1.05 - 1.72 | Reference | Reference | Reference | Reference |
| 1.72 - 3.13 | 0.03 (-0.03, 0.09) | 0.02 (-0.04, 0.08) | 0.02 (-0.04, 0.08) | 0.02 (-0.04, 0.07) |

| | | | | |
|---------------------------------|----------------------|----------------------|----------------------|----------------------|
| ≥ 3.13 | 0.01 (-0.04, 0.05) | 0.01 (-0.04, 0.05) | 0.01 (-0.04, 0.05) | 0.01 (-0.04, 0.06) |
| 2nd trimester | | | | |
| < 0.61 | -0.03 (-0.36, 0.31) | -0.06 (-0.39, 0.26) | -0.05 (-0.38, 0.28) | -0.09 (-0.42, 0.24) |
| 0.61 - 1.02 | -0.10 (-0.28, 0.07) | -0.09 (-0.26, 0.08) | -0.09 (-0.26, 0.08) | -0.11 (-0.28, 0.06) |
| 1.02 - 1.63 | Reference | Reference | Reference | Reference |
| 1.63 - 3.15 | -0.03 (-0.11, 0.06) | -0.02 (-0.10, 0.07) | -0.01 (-0.10, 0.07) | -0.02 (-0.10, 0.07) |
| ≥ 3.15 | -0.10 (-0.17, -0.03) | -0.09 (-0.15, -0.02) | -0.09 (-0.15, -0.02) | -0.08 (-0.15, -0.01) |
| 3rd trimester | | | | |
| < 0.69 | 0.05 (-0.26, 0.36) | 0.07 (-0.23, 0.38) | 0.07 (-0.23, 0.38) | 0.06 (-0.26, 0.38) |
| 0.69 - 1.26 | -0.06 (-0.21, 0.09) | -0.05 (-0.19, 0.10) | -0.04 (-0.19, 0.10) | -0.04 (-0.19, 0.11) |
| 1.26 - 2.12 | Reference | Reference | Reference | Reference |
| 2.12 - 3.89 | -0.05 (-0.13, 0.02) | -0.03 (-0.11, 0.04) | -0.03 (-0.11, 0.04) | -0.03 (-0.11, 0.04) |
| ≥ 3.89 | -0.03 (-0.09, 0.03) | -0.01 (-0.07, 0.05) | -0.01 (-0.07, 0.05) | -0.01 (-0.08, 0.05) |

Abbreviations: β , regression coefficient; CI, confidence interval.

Note: These data are also presented in Figure 1; Quintiles of urinary Mn concentrations were categorized based on trimester-specific cut-points.

Model 1: adjusted for gestational age at delivery.

Model 2: adjusted for gestational age at delivery, maternal age at recruitment, parity, pre-pregnancy BMI, alcohol consumption before pregnancy, active smoking before pregnancy, passive smoking during pregnancy, education, folic acid supplementation, physical activity during pregnancy, and infant sex. Models for birth length model was additionally adjusted for maternal and paternal height.

Model 3: adjusted for variables in Model 2 plus anemia, hypertensive disorders of pregnancy, gestational diabetes mellitus.

Model 4: adjusted for variables in Model 2 plus urinary concentrations of vanadium, arsenic, cadmium, and lead ($\mu\text{g/L}$).

Table S5. Associations of SG-adjusted urinary Mn concentrations ($\mu\text{g/L}$) during pregnancy with size at birth among term births.

| | β (95% CI) for quintiles of urinary manganese concentrations ($\mu\text{g/L}$) | | | |
|---|--|----------------------|----------------------|----------------------|
| | Model 1 | Model 2 | Model 3 | Model 4 |
| Birth weight, g | | | | |
| 1st trimester | | | | |
| < 0.57 | 19.5 (-26.3, 65.2) | 1.0 (-43.5, 45.5) | 3.5 (-40.8, 47.7) | -2.9 (-48.6, 42.8) |
| 0.57 - 1.05 | -3.0 (-26.5, 20.5) | -7.2 (-29.8, 15.4) | -5.4 (-27.9, 17.2) | -8.1 (-30.9, 14.7) |
| 1.05 - 1.72 | Reference | Reference | Reference | Reference |
| 1.72 - 3.13 | 0.1 (-11.3, 11.6) | -2.6 (-13.7, 8.5) | -1.9 (-13.0, 9.2) | -2.9 (-14.1, 8.3) |
| ≥ 3.13 | -2.8 (-11.9, 6.4) | -2.8 (-11.7, 6.1) | -2.5 (-11.4, 6.4) | -2.5 (-12.1, 7.1) |
| 2nd trimester | | | | |
| < 0.61 | 1.3 (-62.6, 65.2) | -8.4 (-68.9, 52.1) | -7.7 (-68.1, 52.7) | -7.4 (-69.4, 54.5) |
| 0.61 - 1.02 | -20.3 (-51.8, 11.3) | -20.1 (-50.8, 10.6) | -19.4 (-50.0, 11.3) | -20.0 (-50.7, 10.6) |
| 1.02 - 1.63 | Reference | Reference | Reference | Reference |
| 1.63 - 3.15 | -5.8 (-21.5, 9.9) | -3.6 (-18.7, 11.6) | -3.3 (-18.5, 11.8) | -4.1 (-19.4, 11.2) |
| ≥ 3.15 | -14.9 (-27.5, -2.4) | -12.4 (-24.6, -0.1) | -11.8 (-24.1, 0.4) | -13.2 (-26.9, 0.5) |
| 3rd trimester | | | | |
| < 0.69 | -9.3 (-67.8, 49.3) | -6.6 (-63.2, 49.9) | -7.1 (-63.7, 49.5) | -8.8 (-67.5, 49.8) |
| 0.69 - 1.26 | -31.5 (-59.6, -3.4) | -25.4 (-52.7, 2.0) | -24.5 (-51.8, 2.7) | -25.9 (-53.6, 1.9) |
| 1.26 - 2.12 | Reference | Reference | Reference | Reference |
| 2.12 - 3.89 | -27.2 (-41.3, -13.0) | -22.0 (-35.8, -8.1) | -21.7 (-35.4, -7.9) | -22.0 (-35.8, -8.1) |
| ≥ 3.89 | -16.2 (-27.7, -4.7) | -11.7 (-22.9, -0.5) | -11.5 (-22.6, -0.4) | -11.7 (-23.7, 0.3) |
| Birth length, cm | | | | |
| 1st trimester | | | | |
| < 0.57 | -0.04 (-0.21, 0.13) | -0.08 (-0.25, 0.08) | -0.07 (-0.24, 0.09) | -0.09 (-0.26, 0.08) |
| 0.57 - 1.05 | -0.02 (-0.10, 0.07) | -0.03 (-0.11, 0.05) | -0.02 (-0.10, 0.06) | -0.03 (-0.11, 0.05) |
| 1.05 - 1.72 | Reference | Reference | Reference | Reference |
| 1.72 - 3.13 | -0.02 (-0.06, 0.02) | -0.02 (-0.06, 0.02) | -0.02 (-0.06, 0.02) | -0.02 (-0.06, 0.02) |
| ≥ 3.13 | -0.02 (-0.05, 0.01) | -0.02 (-0.05, 0.02) | -0.01 (-0.05, 0.02) | -0.01 (-0.05, 0.02) |
| 2nd trimester | | | | |
| < 0.61 | -0.03 (-0.28, 0.21) | -0.11 (-0.34, 0.12) | -0.11 (-0.34, 0.12) | -0.10 (-0.34, 0.14) |
| 0.61 - 1.02 | -0.05 (-0.17, 0.07) | -0.05 (-0.16, 0.06) | -0.05 (-0.16, 0.07) | -0.04 (-0.15, 0.07) |
| 1.02 - 1.63 | Reference | Reference | Reference | Reference |
| 1.63 - 3.15 | -0.02 (-0.08, 0.03) | -0.02 (-0.07, 0.04) | -0.02 (-0.07, 0.04) | -0.02 (-0.07, 0.04) |
| ≥ 3.15 | -0.02 (-0.06, 0.03) | -0.02 (-0.06, 0.03) | -0.02 (-0.06, 0.03) | -0.02 (-0.07, 0.03) |
| 3rd trimester | | | | |
| < 0.69 | -0.06 (-0.28, 0.15) | -0.08 (-0.29, 0.12) | -0.09 (-0.29, 0.12) | -0.08 (-0.29, 0.13) |
| 0.69 - 1.26 | -0.10 (-0.20, 0.00) | -0.08 (-0.17, 0.02) | -0.07 (-0.17, 0.02) | -0.08 (-0.18, 0.02) |
| 1.26 - 2.12 | Reference | Reference | Reference | Reference |
| 2.12 - 3.89 | -0.10 (-0.15, -0.05) | -0.08 (-0.13, -0.03) | -0.08 (-0.13, -0.03) | -0.08 (-0.13, -0.03) |
| ≥ 3.89 | -0.06 (-0.10, -0.02) | -0.05 (-0.08, -0.01) | -0.05 (-0.08, -0.01) | -0.04 (-0.09, 0.00) |
| Ponderal index, kg/m^3 | | | | |
| 1st trimester | | | | |
| < 0.57 | 0.24 (0.00, 0.48) | 0.19 (-0.05, 0.43) | 0.20 (-0.04, 0.44) | 0.16 (-0.08, 0.41) |
| 0.57 - 1.05 | 0.01 (-0.11, 0.13) | -0.01 (-0.13, 0.11) | 0.00 (-0.12, 0.12) | -0.02 (-0.14, 0.10) |
| 1.05 - 1.72 | Reference | Reference | Reference | Reference |
| 1.72 - 3.13 | 0.04 (-0.02, 0.10) | 0.03 (-0.03, 0.09) | 0.03 (-0.03, 0.09) | 0.02 (-0.04, 0.08) |

| | | | | |
|---------------------------------|----------------------|----------------------|----------------------|---------------------|
| ≥ 3.13 | 0.01 (-0.04, 0.06) | 0.01 (-0.04, 0.06) | 0.01 (-0.04, 0.06) | 0.01 (-0.04, 0.06) |
| 2nd trimester | | | | |
| < 0.61 | 0.03 (-0.30, 0.37) | -0.01 (-0.34, 0.32) | 0.00 (-0.33, 0.33) | -0.03 (-0.37, 0.30) |
| 0.61 - 1.02 | -0.07 (-0.25, 0.11) | -0.07 (-0.25, 0.10) | -0.07 (-0.24, 0.10) | -0.09 (-0.26, 0.08) |
| 1.02 - 1.63 | Reference | Reference | Reference | Reference |
| 1.63 - 3.15 | -0.01 (-0.10, 0.08) | 0.00 (-0.08, 0.08) | 0.00 (-0.08, 0.09) | 0.00 (-0.09, 0.08) |
| ≥ 3.15 | -0.09 (-0.16, -0.02) | -0.08 (-0.15, -0.01) | -0.08 (-0.14, -0.01) | -0.07 (-0.15, 0.00) |
| 3rd trimester | | | | |
| < 0.69 | 0.03 (-0.28, 0.34) | 0.05 (-0.25, 0.36) | 0.06 (-0.24, 0.36) | 0.05 (-0.27, 0.36) |
| 0.69 - 1.26 | -0.08 (-0.23, 0.07) | -0.06 (-0.21, 0.08) | -0.06 (-0.20, 0.09) | -0.06 (-0.21, 0.09) |
| 1.26 - 2.12 | Reference | Reference | Reference | Reference |
| 2.12 - 3.89 | -0.06 (-0.13, 0.02) | -0.04 (-0.11, 0.04) | -0.04 (-0.11, 0.04) | -0.04 (-0.11, 0.04) |
| ≥ 3.89 | -0.03 (-0.09, 0.03) | -0.01 (-0.07, 0.05) | -0.01 (-0.07, 0.05) | -0.02 (-0.08, 0.05) |

Abbreviations: β , regression coefficient; CI, confidence interval.

Note: Quintiles of urinary Mn concentrations were categorized based on trimester-specific cut-points.

Model 1: adjusted for gestational age at delivery.

Model 2: adjusted for gestational age at delivery, maternal age at recruitment, parity, pre-pregnancy BMI, alcohol consumption before pregnancy, active smoking before pregnancy, passive smoking during pregnancy, education, folic acid supplementation, physical activity during pregnancy, and infant sex. Models for birth length model was additionally adjusted for maternal and paternal height.

Model 3: adjusted for variables in Model 2 plus anemia, hypertensive disorders of pregnancy, gestational diabetes mellitus.

Model 4: adjusted for variables in Model 2 plus urinary concentrations of vanadium, arsenic, cadmium, and lead ($\mu\text{g/L}$).

Table S6. Adjusted associations of SG-adjusted urinary Mn concentrations ($\mu\text{g/L}$) during pregnancy with size at birth among women without pregnancy complications.

| Manganese ($\mu\text{g/L}$) | Adjusted β (95% CI) for all participants (n = 2537) | | | Adjusted β (95% CI) for term births (n = 2497) | | |
|---------------------------------|---|----------------------|---------------------------------|--|----------------------|---------------------------------|
| | Birth weight, g | Birth length, cm | Ponderal index, kg/m^3 | Birth weight, g | Birth length, cm | Ponderal index, kg/m^3 |
| 1st trimester | | | | | | |
| < 0.57 | -14.2 (-60.4, 32.0) | -0.15 (-0.33, 0.03) | 0.19 (-0.06, 0.45) | -13.1 (-59.9, 33.7) | -0.15 (-0.32, 0.03) | 0.20 (-0.06, 0.45) |
| 0.57 - 1.05 | -13.5 (-36.8, 9.7) | -0.01 (-0.10, 0.07) | -0.06 (-0.19, 0.06) | -13.0 (-36.6, 10.7) | -0.02 (-0.10, 0.07) | -0.06 (-0.18, 0.07) |
| 1.05 - 1.72 | Reference | Reference | Reference | Reference | Reference | Reference |
| 1.72 - 3.13 | -4.4 (-15.9, 7.1) | -0.02 (-0.07, 0.02) | 0.01 (-0.05, 0.08) | -2.2 (-13.8, 9.5) | -0.02 (-0.06, 0.02) | 0.03 (-0.03, 0.09) |
| ≥ 3.13 | -2.2 (-11.7, 7.3) | -0.01 (-0.05, 0.02) | 0.01 (-0.04, 0.06) | -1.9 (-11.4, 7.7) | -0.01 (-0.05, 0.02) | 0.02 (-0.03, 0.07) |
| 2nd trimester | | | | | | |
| < 0.61 | -27.1 (-90.8, 36.6) | -0.16 (-0.40, 0.09) | -0.08 (-0.43, 0.27) | -23.8 (-88.1, 40.4) | -0.18 (-0.43, 0.07) | -0.03 (-0.38, 0.32) |
| 0.61 - 1.02 | -17.0 (-48.8, 14.9) | -0.03 (-0.15, 0.09) | -0.08 (-0.26, 0.10) | -14.6 (-46.8, 17.7) | -0.03 (-0.16, 0.09) | -0.06 (-0.24, 0.12) |
| 1.02 - 1.63 | Reference | Reference | Reference | Reference | Reference | Reference |
| 1.63 - 3.15 | -3.0 (-18.9, 12.8) | -0.02 (-0.08, 0.04) | 0.01 (-0.08, 0.10) | -2.8 (-18.8, 13.2) | -0.03 (-0.09, 0.03) | 0.02 (-0.07, 0.11) |
| ≥ 3.15 | -13.1 (-25.9, -0.2) | -0.01 (-0.06, 0.03) | -0.09 (-0.16, -0.02) | -12.0 (-25.0, 1.0) | -0.01 (-0.06, 0.03) | -0.08 (-0.15, -0.02) |
| 3rd trimester | | | | | | |
| < 0.69 | -8.8 (-67.2, 49.7) | -0.10 (-0.32, 0.12) | 0.07 (-0.25, 0.39) | -9.9 (-68.9, 49.1) | -0.12 (-0.34, 0.11) | 0.07 (-0.25, 0.39) |
| 0.69 - 1.26 | -32.8 (-61.3, -4.3) | -0.09 (-0.19, 0.02) | -0.10 (-0.25, 0.06) | -34.3 (-63.1, -5.6) | -0.10 (-0.20, 0.01) | -0.10 (-0.26, 0.06) |
| 1.26 - 2.12 | Reference | Reference | Reference | Reference | Reference | Reference |
| 2.12 - 3.89 | -21.3 (-35.5, -7.2) | -0.07 (-0.12, -0.02) | -0.05 (-0.13, 0.03) | -21.6 (-36.0, -7.3) | -0.07 (-0.12, -0.01) | -0.05 (-0.13, 0.03) |
| ≥ 3.89 | -11.9 (-23.2, -0.7) | -0.03 (-0.08, 0.01) | -0.03 (-0.09, 0.04) | -11.8 (-23.2, -0.4) | -0.03 (-0.08, 0.01) | -0.03 (-0.09, 0.04) |

Abbreviations: β , regression coefficient; CI, confidence interval.

Note: Quintiles of urinary Mn concentrations were categorized based on trimester-specific cut-points.

Models were adjusted for gestational age at delivery, maternal age at recruitment, parity, pre-pregnancy BMI, alcohol consumption before pregnancy, active smoking before pregnancy, passive smoking during pregnancy, education, folic acid supplementation, physical activity during pregnancy, and infant sex. Models for birth length model was additionally adjusted for maternal and paternal height.

Table S7. Adjusted associations of SG-adjusted urinary Mn concentrations ($\mu\text{g/L}$) during pregnancy with size at birth among women who provided completed three urine samples.

| Manganese ($\mu\text{g/L}$) | Adjusted β (95% CI) for all participants (n = 857) | | | Adjusted β (95% CI) for term births (n = 844) | | |
|----------------------------------|--|----------------------|---------------------------------|---|----------------------|---------------------------------|
| | Birth weight, g | Birth length, cm | Ponderal index, kg/m^3 | Birth weight, g | Birth length, cm | Ponderal index, kg/m^3 |
| 1st trimester | | | | | | |
| < 0.57 | 3.3 (-70.8, 77.5) | 0.01 (-0.26, 0.29) | 0.04 (-0.35, 0.44) | 12.6 (-60.9, 86.0) | 0.02 (-0.25, 0.30) | 0.11 (-0.28, 0.50) |
| 0.57 - 1.05 | -10.2 (-49.3, 28.8) | 0.06 (-0.08, 0.19) | -0.17 (-0.37, 0.04) | -8.4 (-47.5, 30.6) | 0.04 (-0.10, 0.18) | -0.14 (-0.34, 0.07) |
| 1.05 - 1.72 | Reference | Reference | Reference | Reference | Reference | Reference |
| 1.72 - 3.13 | 1.0 (-21.1, 23.1) | 0.04 (-0.05, 0.12) | -0.03 (-0.15, 0.08) | 1.3 (-20.8, 23.5) | 0.03 (-0.05, 0.12) | -0.02 (-0.14, 0.09) |
| ≥ 3.13 | -5.0 (-21.7, 11.8) | 0.00 (-0.06, 0.06) | -0.02 (-0.11, 0.07) | -4.3 (-21.0, 12.4) | -0.01 (-0.07, 0.06) | -0.01 (-0.10, 0.08) |
| 2nd trimester | | | | | | |
| < 0.61 | 39.3 (-35.0, 113.5) | 0.00 (-0.28, 0.28) | 0.15 (-0.25, 0.56) | 43.1 (-30.9, 117.0) | -0.02 (-0.30, 0.26) | 0.21 (-0.20, 0.61) |
| 0.61 - 1.02 | -27.6 (-65.4, 10.2) | -0.05 (-0.18, 0.09) | -0.17 (-0.38, 0.04) | -26.5 (-63.9, 10.9) | -0.05 (-0.19, 0.09) | -0.16 (-0.37, 0.05) |
| 1.02 - 1.63 | Reference | Reference | Reference | Reference | Reference | Reference |
| 1.63 - 3.15 | -1.7 (-22.1, 18.7) | -0.02 (-0.10, 0.05) | 0.01 (-0.10, 0.12) | 1.4 (-18.8, 21.5) | -0.02 (-0.09, 0.05) | 0.03 (-0.07, 0.14) |
| ≥ 3.15 | -9.8 (-25.4, 5.8) | -0.01 (-0.06, 0.05) | -0.07 (-0.15, 0.02) | -8.6 (-24.1, 6.9) | -0.01 (-0.06, 0.05) | -0.06 (-0.14, 0.03) |
| 3rd trimester | | | | | | |
| < 0.69 | 22.2 (-55.8, 100.2) | -0.13 (-0.42, 0.17) | 0.32 (-0.11, 0.74) | 6.2 (-70.8, 83.3) | -0.17 (-0.46, 0.13) | 0.23 (-0.19, 0.66) |
| 0.69 - 1.26 | -36.7 (-75.0, 1.7) | -0.17 (-0.32, -0.02) | -0.01 (-0.22, 0.20) | -42.0 (-80.2, -3.9) | -0.19 (-0.33, -0.04) | -0.04 (-0.25, 0.17) |
| 1.26 - 2.12 | Reference | Reference | Reference | Reference | Reference | Reference |
| 2.12 - 3.89 | -20.9 (-41.4, -0.5) | -0.13 (-0.21, -0.05) | 0.05 (-0.07, 0.16) | -23.2 (-43.5, -2.9) | -0.13 (-0.21, -0.05) | 0.03 (-0.08, 0.15) |
| ≥ 3.89 | -11.3 (-29.3, 6.6) | -0.06 (-0.13, 0.00) | 0.01 (-0.08, 0.10) | -12.6 (-30.6, 5.5) | -0.07 (-0.13, 0.00) | 0.00 (-0.09, 0.09) |

Abbreviations: β , regression coefficient; CI, confidence interval.

Note: Quintiles of urinary Mn concentrations were categorized based on trimester-specific cut-points.

Models were adjusted for gestational age at delivery, maternal age at recruitment, parity, pre-pregnancy BMI, alcohol consumption before pregnancy, active smoking before pregnancy, passive smoking during pregnancy, education, folic acid supplementation, physical activity during pregnancy, and infant sex. Models for birth length model was additionally adjusted for maternal and paternal height.

Table S8. Adjusted associations of overall quintiles for SG-adjusted urinary Mn concentrations ($\mu\text{g/L}$) during pregnancy with size at birth.

| Manganese ($\mu\text{g/L}$) | Adjusted β (95% CI) for all participants (n = 3022) | | | Adjusted β (95% CI) for term births (n = 2923) | | |
|----------------------------------|---|---------------------|---------------------------------|--|---------------------|---------------------------------|
| | Birth weight, g | Birth length, cm | Ponderal index, kg/m^3 | Birth weight, g | Birth length, cm | Ponderal index, kg/m^3 |
| 1st trimester | | | | | | |
| < 0.61 | 7.1 (-35.6, 49.9) | -0.06 (-0.22, 0.10) | 0.21 (-0.01, 0.44) | 7.1 (-35.9, 50.2) | -0.07 (-0.23, 0.09) | 0.22 (-0.01, 0.45) |
| 0.61 - 1.09 | -5.9 (-28.0, 16.2) | -0.01 (-0.09, 0.07) | -0.02 (-0.13, 0.10) | -6.1 (-28.5, 16.3) | -0.01 (-0.09, 0.07) | -0.02 (-0.13, 0.10) |
| 1.09 - 1.80 | Reference | Reference | Reference | Reference | Reference | Reference |
| 1.80 - 3.29 | 0.1 (-10.7, 11.0) | -0.02 (-0.06, 0.02) | 0.03 (-0.02, 0.09) | 0.3 (-10.7, 11.4) | -0.02 (-0.06, 0.02) | 0.04 (-0.02, 0.10) |
| ≥ 3.29 | -1.3 (-10.2, 7.6) | -0.01 (-0.04, 0.03) | 0.01 (-0.04, 0.06) | -1.4 (-10.4, 7.6) | -0.01 (-0.04, 0.02) | 0.01 (-0.03, 0.06) |
| 2nd trimester | | | | | | |
| < 0.61 | 3.5 (-57.2, 64.2) | -0.08 (-0.32, 0.15) | 0.06 (-0.26, 0.38) | 11.2 (-49.9, 72.4) | -0.06 (-0.30, 0.17) | 0.10 (-0.22, 0.43) |
| 0.61 - 1.09 | -9.1 (-38.4, 20.3) | -0.03 (-0.14, 0.08) | 0.00 (-0.17, 0.16) | -6.0 (-35.8, 23.7) | -0.02 (-0.13, 0.10) | 0.01 (-0.16, 0.17) |
| 1.09 - 1.80 | Reference | Reference | Reference | Reference | Reference | Reference |
| 1.80 - 3.29 | 2.1 (-13.2, 17.5) | 0.01 (-0.05, 0.06) | 0.01 (-0.07, 0.10) | 3.4 (-12.0, 18.8) | 0.01 (-0.05, 0.06) | 0.03 (-0.06, 0.11) |
| ≥ 3.29 | -10.3 (-22.8, 2.1) | -0.01 (-0.06, 0.03) | -0.07 (-0.13, 0.00) | -8.9 (-21.5, 3.7) | -0.01 (-0.05, 0.04) | -0.06 (-0.13, 0.01) |
| 3rd trimester | | | | | | |
| < 0.61 | 7.6 (-52.1, 67.4) | 0.02 (-0.20, 0.23) | 0.07 (-0.25, 0.39) | -3.0 (-62.6, 56.6) | -0.02 (-0.24, 0.20) | 0.03 (-0.29, 0.34) |
| 0.61 - 1.09 | -5.3 (-33.5, 23.0) | -0.06 (-0.17, 0.04) | 0.09 (-0.06, 0.24) | -8.4 (-36.6, 19.7) | -0.07 (-0.17, 0.03) | 0.07 (-0.08, 0.22) |
| 1.09 - 1.80 | Reference | Reference | Reference | Reference | Reference | Reference |
| 1.80 - 3.29 | -12.3 (-26.3, 1.7) | -0.05 (-0.10, 0.00) | -0.01 (-0.08, 0.07) | -14.2 (-28.2, -0.1) | -0.05 (-0.10, 0.00) | -0.02 (-0.09, 0.06) |
| ≥ 3.29 | -8.3 (-19.2, 2.5) | -0.03 (-0.07, 0.01) | 0.00 (-0.06, 0.06) | -9.2 (-20.0, 1.6) | -0.03 (-0.07, 0.00) | 0.00 (-0.06, 0.05) |

Abbreviations: β , regression coefficient; CI, confidence interval.

Note: Quintiles of urinary Mn concentration were categorized by pooling measurements from all trimesters

Models were adjusted for gestational age at delivery, maternal age at recruitment, parity, pre-pregnancy BMI, alcohol consumption before pregnancy, active smoking before pregnancy, passive smoking during pregnancy, education, folic acid supplementation, physical activity during pregnancy, and infant sex. Models for birth length model was additionally adjusted for maternal and paternal height.

Table S9. Adjusted associations of unadjusted urinary Mn concentrations ($\mu\text{g/L}$) during pregnancy with size at birth.

| Manganese ($\mu\text{g/L}$) | Adjusted β (95% CI) for all participants (n = 3022) | | | Adjusted β (95% CI) for term births (n = 2923) | | |
|----------------------------------|---|---------------------|---------------------------------|--|---------------------|---------------------------------|
| | Birth weight, g | Birth length, cm | Ponderal index, kg/m^3 | Birth weight, g | Birth length, cm | Ponderal index, kg/m^3 |
| 1st trimester | | | | | | |
| < 0.57 | 1.3 (-42.2, 44.8) | -0.06 (-0.23, 0.10) | 0.17 (-0.07, 0.40) | 0.5 (-43.6, 44.6) | -0.04 (-0.21, 0.12) | 0.12 (-0.11, 0.36) |
| 0.57 - 1.05 | -11.6 (-34.0, 10.7) | -0.03 (-0.11, 0.06) | -0.02 (-0.13, 0.09) | -11.4 (-34.0, 11.2) | -0.01 (-0.10, 0.07) | -0.04 (-0.15, 0.08) |
| 1.05 - 1.72 | Reference | Reference | Reference | Reference | Reference | Reference |
| 1.72 - 3.13 | -7.4 (-18.3, 3.5) | -0.01 (-0.05, 0.04) | -0.04 (-0.09, 0.02) | -6.9 (-17.9, 4.2) | 0.00 (-0.04, 0.04) | -0.04 (-0.10, 0.02) |
| ≥ 3.13 | -2.5 (-11.5, 6.4) | -0.01 (-0.04, 0.02) | 0.00 (-0.05, 0.04) | -2.0 (-11.1, 7.1) | 0.00 (-0.04, 0.03) | 0.00 (-0.05, 0.05) |
| 2nd trimester | | | | | | |
| < 0.61 | -8.3 (-68.0, 51.5) | -0.20 (-0.44, 0.03) | 0.15 (-0.17, 0.46) | 5.6 (-55.3, 66.5) | -0.16 (-0.40, 0.08) | 0.20 (-0.12, 0.52) |
| 0.61 - 1.02 | -0.4 (-30.0, 29.2) | -0.03 (-0.15, 0.08) | 0.07 (-0.10, 0.23) | -1.0 (-31.0, 29.1) | -0.04 (-0.16, 0.07) | 0.08 (-0.09, 0.24) |
| 1.02 - 1.63 | Reference | Reference | Reference | Reference | Reference | Reference |
| 1.63 - 3.15 | -8.3 (-23.6, 6.9) | -0.03 (-0.09, 0.02) | -0.02 (-0.10, 0.07) | -6.3 (-21.7, 9.2) | -0.03 (-0.09, 0.03) | 0.00 (-0.09, 0.08) |
| ≥ 3.15 | -8.8 (-20.9, 3.2) | -0.03 (-0.07, 0.02) | -0.03 (-0.10, 0.03) | -7.8 (-20.0, 4.5) | -0.03 (-0.07, 0.02) | -0.02 (-0.09, 0.04) |
| 3rd trimester | | | | | | |
| < 0.69 | 35.4 (-18.4, 89.1) | 0.01 (-0.19, 0.21) | 0.26 (-0.03, 0.55) | 28.2 (-25.3, 81.6) | -0.01 (-0.21, 0.19) | 0.22 (-0.07, 0.51) |
| 0.69 - 1.26 | 18.7 (-8.7, 46.0) | -0.01 (-0.11, 0.09) | 0.15 (0.01, 0.30) | 13.7 (-13.7, 41.1) | -0.02 (-0.12, 0.08) | 0.13 (-0.02, 0.27) |
| 1.26 - 2.12 | Reference | Reference | Reference | Reference | Reference | Reference |
| 2.12 - 3.89 | 7.7 (-5.9, 21.3) | -0.01 (-0.06, 0.04) | 0.08 (0.00, 0.15) | 6.7 (-6.9, 20.3) | -0.01 (-0.06, 0.03) | 0.07 (0.00, 0.14) |
| ≥ 3.89 | 2.5 (-8.1, 13.1) | -0.02 (-0.06, 0.02) | 0.06 (0.00, 0.12) | 1.3 (-9.3, 12.0) | -0.03 (-0.07, 0.01) | 0.05 (-0.01, 0.11) |

Abbreviations: β , regression coefficient; CI, confidence interval.

Note: Quintiles of urinary Mn concentrations were categorized based on trimester-specific cut-points.

Models were adjusted for gestational age at delivery, maternal age at recruitment, parity, pre-pregnancy BMI, alcohol consumption before pregnancy, active smoking before pregnancy, passive smoking during pregnancy, education, folic acid supplementation, physical activity during pregnancy, and infant sex. Models for birth length model was additionally adjusted for maternal and paternal height.

Table S10. Adjusted associations of SG-adjusted urinary Mn concentrations ($\mu\text{g/L}$) during pregnancy with size at birth, stratified by infant sex and maternal age at recruitment.

| Manganese ($\mu\text{g/L}$) | Adjusted β (95% CI) stratified by infant sex | | | Adjusted β (95% CI) stratified by maternal age | | |
|---------------------------------|--|----------------------|-------------------------|--|-----------------------------|-------------------------|
| | Boys (n = 1594) | Girls (n = 1428) | P-value for interaction | ≤ 27 years old (n = 1601) | > 27 years old (n = 1421) | P-value for interaction |
| Birth weight, g | | | | | | |
| 1st trimester | | | | | | |
| < 0.57 | 5.1 (-55.9, 66.1) | -13.2 (-77.7, 51.3) | 0.7082 | -2.1 (-61.2, 57.0) | 5.2 (-61.3, 71.7) | 0.7951 |
| 0.57 - 1.05 | -10.8 (-41.2, 19.7) | -4.9 (-37.3, 27.4) | 0.8053 | -15.5 (-44.3, 13.3) | 0.0 (-34.6, 34.5) | 0.4572 |
| 1.05 - 1.72 | Reference | Reference | - | Reference | Reference | - |
| 1.72 - 3.13 | -9.5 (-24.7, 5.6) | 3.3 (-12.4, 18.9) | 0.2483 | -7.8 (-22.5, 6.9) | 1.6 (-14.7, 17.8) | 0.4018 |
| ≥ 3.13 | -9.3 (-21.0, 2.5) | 2.7 (-10.5, 15.9) | 0.1796 | 2.9 (-9.4, 15.3) | -9.2 (-21.7, 3.2) | 0.1667 |
| 2nd trimester | | | | | | |
| < 0.61 | 28.9 (-52.8, 110.6) | -60.8 (-148.2, 26.7) | 0.1232 | -37.2 (-119.0, 44.6) | 0.7 (-86.7, 88.0) | 0.5418 |
| 0.61 - 1.02 | -22.3 (-63.9, 19.3) | -20.8 (-65.8, 24.1) | 0.9847 | -34.7 (-76.5, 7.1) | -7.5 (-51.7, 36.7) | 0.4456 |
| 1.02 - 1.63 | Reference | Reference | - | Reference | Reference | - |
| 1.63 - 3.15 | 3.1 (-17.3, 23.6) | -13.4 (-35.8, 9.0) | 0.2892 | -11.2 (-30.9, 8.4) | 1.8 (-21.5, 25.1) | 0.3706 |
| ≥ 3.15 | -15.6 (-31.6, 0.4) | -9.1 (-27.8, 9.6) | 0.5550 | -12.7 (-30.1, 4.7) | -13.7 (-30.6, 3.3) | 0.8948 |
| 3rd trimester | | | | | | |
| < 0.69 | 14.1 (-58.2, 86.4) | -22.4 (-111.0, 66.2) | 0.5582 | -25.2 (-103.2, 52.7) | 20.6 (-60.8, 102.0) | 0.4337 |
| 0.69 - 1.26 | -39.2 (-76.6, -1.7) | -5.1 (-45.1, 35.0) | 0.2473 | -26.0 (-64.6, 12.6) | -21.2 (-59.6, 17.2) | 0.9310 |
| 1.26 - 2.12 | Reference | Reference | - | Reference | Reference | - |
| 2.12 - 3.89 | -25.5 (-44.2, -6.7) | -15.5 (-35.8, 4.8) | 0.6098 | -24.2 (-43.7, -4.7) | -18.3 (-37.7, 1.1) | 0.7712 |
| ≥ 3.89 | -10.8 (-25.9, 4.4) | -11.2 (-27.6, 5.2) | 0.8168 | -11.6 (-26.7, 3.5) | -9.8 (-26.1, 6.4) | 0.9071 |
| Birth length, cm | | | | | | |
| 1st trimester | | | | | | |
| < 0.57 | -0.09 (-0.31, 0.13) | -0.08 (-0.34, 0.18) | 0.9071 | -0.05 (-0.27, 0.17) | -0.09 (-0.34, 0.16) | 0.8909 |
| 0.57 - 1.05 | -0.04 (-0.15, 0.07) | -0.01 (-0.13, 0.10) | 0.7532 | -0.05 (-0.16, 0.05) | -0.01 (-0.13, 0.12) | 0.4840 |
| 1.05 - 1.72 | Reference | Reference | - | Reference | Reference | - |
| 1.72 - 3.13 | -0.02 (-0.07, 0.03) | -0.03 (-0.09, 0.03) | 0.8090 | -0.02 (-0.07, 0.04) | -0.03 (-0.09, 0.03) | 0.8941 |
| ≥ 3.13 | -0.02 (-0.06, 0.03) | -0.01 (-0.06, 0.04) | 0.8290 | 0.00 (-0.05, 0.04) | -0.02 (-0.06, 0.03) | 0.7039 |
| 2nd trimester | | | | | | |
| < 0.61 | 0.03 (-0.29, 0.35) | -0.25 (-0.59, 0.09) | 0.1706 | -0.18 (-0.49, 0.13) | -0.08 (-0.42, 0.27) | 0.4933 |
| 0.61 - 1.02 | -0.01 (-0.16, 0.15) | -0.08 (-0.25, 0.08) | 0.4237 | -0.07 (-0.22, 0.08) | 0.01 (-0.16, 0.18) | 0.5243 |
| 1.02 - 1.63 | Reference | Reference | - | Reference | Reference | - |

| | | | | | | |
|---|----------------------|----------------------|--------|----------------------|----------------------|--------|
| 1.63 - 3.15 | 0.04 (-0.04, 0.12) | -0.06 (-0.14, 0.02) | 0.0735 | 0.00 (-0.07, 0.07) | -0.03 (-0.12, 0.06) | 0.5951 |
| ≥ 3.15 | 0.00 (-0.06, 0.06) | -0.03 (-0.09, 0.04) | 0.5801 | -0.01 (-0.07, 0.06) | -0.02 (-0.08, 0.04) | 0.6178 |
| 3rd trimester | | | | | | |
| < 0.69 | -0.01 (-0.29, 0.26) | -0.15 (-0.45, 0.15) | 0.4396 | -0.08 (-0.35, 0.20) | -0.03 (-0.33, 0.26) | 0.7634 |
| 0.69 - 1.26 | -0.07 (-0.21, 0.07) | -0.09 (-0.23, 0.05) | 0.7534 | -0.10 (-0.23, 0.04) | -0.06 (-0.20, 0.09) | 0.8024 |
| 1.26 - 2.12 | Reference | Reference | - | Reference | Reference | - |
| 2.12 - 3.89 | -0.07 (-0.14, 0.00) | -0.09 (-0.16, -0.01) | 0.5601 | -0.07 (-0.13, 0.00) | -0.08 (-0.16, -0.01) | 0.6796 |
| ≥ 3.89 | -0.04 (-0.09, 0.02) | -0.05 (-0.11, 0.00) | 0.6438 | -0.03 (-0.08, 0.03) | -0.05 (-0.11, 0.00) | 0.4021 |
| Ponderal index, kg/m³ | | | | | | |
| 1st trimester | | | | | | |
| < 0.57 | 0.30 (-0.01, 0.62) | 0.02 (-0.33, 0.38) | 0.2905 | 0.07 (-0.26, 0.39) | 0.31 (-0.04, 0.66) | 0.3190 |
| 0.57 - 1.05 | 0.00 (-0.16, 0.16) | -0.03 (-0.20, 0.14) | 0.8439 | -0.03 (-0.18, 0.13) | 0.00 (-0.18, 0.18) | 0.8672 |
| 1.05 - 1.72 | Reference | Reference | - | Reference | Reference | - |
| 1.72 - 3.13 | -0.03 (-0.10, 0.05) | 0.07 (-0.02, 0.15) | 0.1077 | -0.03 (-0.11, 0.05) | 0.08 (-0.01, 0.16) | 0.0741 |
| ≥ 3.13 | -0.02 (-0.08, 0.04) | 0.04 (-0.04, 0.11) | 0.2229 | 0.03 (-0.04, 0.09) | -0.02 (-0.09, 0.05) | 0.2930 |
| 2nd trimester | | | | | | |
| < 0.61 | 0.06 (-0.36, 0.48) | -0.22 (-0.73, 0.29) | 0.4041 | -0.03 (-0.51, 0.44) | -0.09 (-0.54, 0.36) | 0.7800 |
| 0.61 - 1.02 | -0.12 (-0.35, 0.11) | -0.08 (-0.33, 0.18) | 0.7428 | -0.17 (-0.42, 0.08) | -0.04 (-0.28, 0.19) | 0.5676 |
| 1.02 - 1.63 | Reference | Reference | - | Reference | Reference | - |
| 1.63 - 3.15 | -0.02 (-0.13, 0.10) | -0.03 (-0.15, 0.10) | 0.9286 | -0.08 (-0.19, 0.03) | 0.04 (-0.08, 0.17) | 0.1271 |
| ≥ 3.15 | -0.12 (-0.20, -0.04) | -0.05 (-0.16, 0.06) | 0.2747 | -0.10 (-0.19, -0.01) | -0.07 (-0.17, 0.02) | 0.6134 |
| 3rd trimester | | | | | | |
| < 0.69 | 0.09 (-0.29, 0.46) | 0.07 (-0.43, 0.57) | 0.8723 | -0.02 (-0.45, 0.40) | 0.13 (-0.30, 0.57) | 0.6192 |
| 0.69 - 1.26 | -0.20 (-0.39, -0.01) | 0.13 (-0.10, 0.37) | 0.0210 | -0.01 (-0.22, 0.19) | -0.09 (-0.30, 0.12) | 0.6099 |
| 1.26 - 2.12 | Reference | Reference | - | Reference | Reference | - |
| 2.12 - 3.89 | -0.07 (-0.17, 0.03) | 0.02 (-0.10, 0.13) | 0.2166 | -0.07 (-0.17, 0.04) | 0.00 (-0.10, 0.10) | 0.4696 |
| ≥ 3.89 | -0.01 (-0.09, 0.06) | 0.00 (-0.09, 0.09) | 0.8506 | -0.03 (-0.11, 0.05) | 0.00 (-0.09, 0.08) | 0.8769 |

Abbreviations: β , regression coefficient; CI, confidence interval.

Note: These data are also presented in Figure 2; Quintiles of urinary Mn concentrations were categorized based on trimester-specific cut-points; Stratum-specific *P*-values for interaction were estimated as the *P*-values for the interaction terms of infant sex (or maternal age) and each quintile of urinary Mn concentrations.

Models were adjusted for gestational age at delivery, maternal age at recruitment, parity, pre-pregnancy BMI, alcohol consumption before pregnancy, active smoking before pregnancy, passive smoking during pregnancy, education, folic acid supplementation, physical activity during pregnancy, and infant sex. Models for birth length model was additionally adjusted for maternal and paternal height.

Figure S1. Relative exposure of Mn comparing newborns in the 10th percentile of birth weight, birth length, or Ponderal index with those in the 90th percentile among term births.

Solid lines represent relative exposures of Mn through the whole pregnancy, comparing newborns in the 10th percentiles of A) birth weight, B) birth length, or C) Ponderal index to those in the 90th percentiles. Dotted lines represent pointwise 95% confidence intervals. Models were adjusted for gestational age at delivery, maternal age at recruitment, parity, pre-pregnancy BMI, alcohol consumption before pregnancy, active smoking before pregnancy, passive smoking during pregnancy, education, folic acid supplementation, physical activity during pregnancy, and infant sex. The model for birth length model was additionally adjusted for maternal and paternal height.

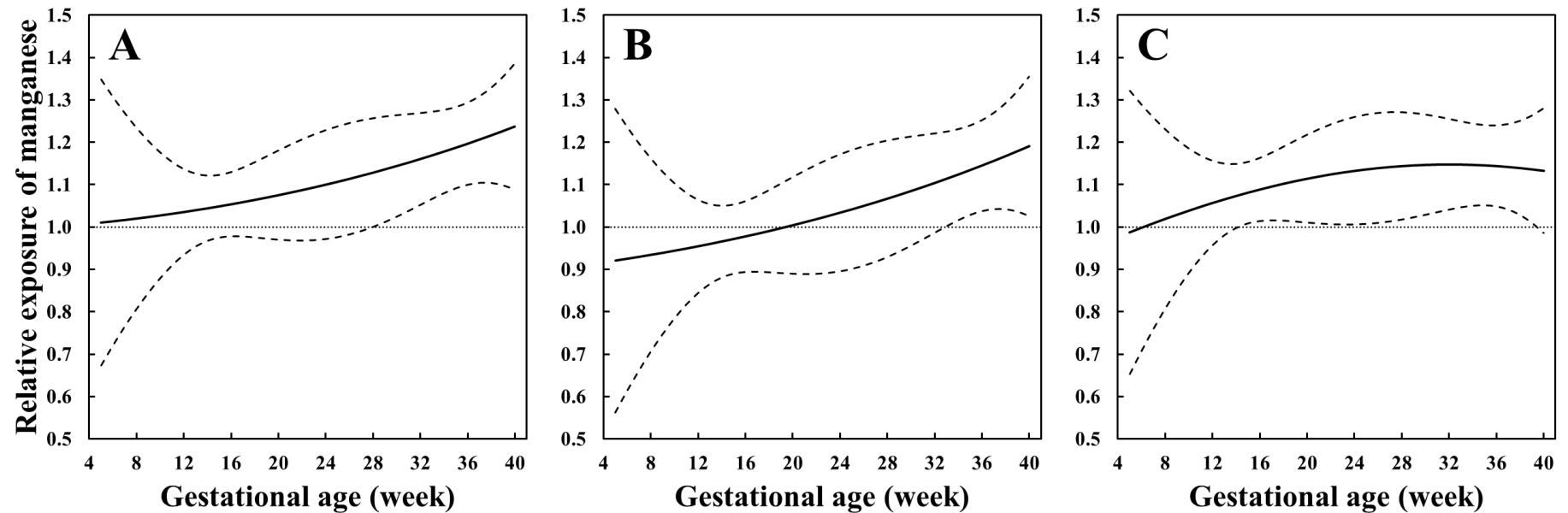


Figure S2. Relative exposure of Mn comparing newborns in the 10th percentile of birth weight, birth length, or Ponderal index with those in the 90th percentile among women who provided completed three urine samples.

Solid lines represent relative exposures of Mn through the whole pregnancy, comparing newborns in the 10th percentiles of A) birth weight, B) birth length, or C) Ponderal index to those in the 90th percentiles. Dotted lines represent pointwise 95% confidence intervals. Models were adjusted for gestational age at delivery, maternal age at recruitment, parity, pre-pregnancy BMI, alcohol consumption before pregnancy, active smoking before pregnancy, passive smoking during pregnancy, education, folic acid supplementation, physical activity during pregnancy, and infant sex. The model for birth length model was additionally adjusted for maternal and paternal height.

