Supplemental Material

Prenatal Arsenic Exposure and Birth Outcomes among a Population Residing near a Mining-Related Superfund Site

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Table S1. Adjusted associations[a] of blood arsenic with birth outcomes

Exposure	Birth Weight (g)		Gestational Age (weeks)		Birth Weight for Gestational Age (z-score)		Head Circumference (cm)	
	n	Estimate (95% CI)[b]	n	Estimate (95% CI)[b]	n	Estimate (95% CI)[b]	n	Estimate (95% CI)[b]
Maternal blood arsenic								
Quartile 1[c]	151	0 (reference)	151	0 (reference)	151	0 (reference)	146	0 (reference)
Quartile 2	145	-20.0 (-124.7, 84.8)	145	0.02 (-0.27, 0.31)	145	-0.06 (-0.27, 0.16)	138	0.00 (-0.41, 0.41)
Quartile 3	151	-78.4 (-182.4, 25.7)	151	-0.16 (-0.45, 0.13)	151	-0.11 (-0.32, 0.10)	144	-0.44 (-0.85, -0.04)
Quartile 4	149	-142.5 (-252.9, -32.2)	149	-0.41 (-0.72, -0.11)	149	-0.21 (-0.43, 0.01)	146	-0.48 (-0.91, -0.05)
Per IQR increase	596	-77.5 (-127.8, -27.3)	596	-0.13 (-0.27, 0.01)	596	-0.14 (-0.24, -0.04)	574	-0.22 (-0.42, -0.03)
Cord blood arsenic								
Quartile 1[d]	139	0 (reference)	139	0 (reference)	139	0 (reference)	135	0 (reference)
Quartile 2	151	78.5 (-28.8, 185.8)	151	0.30 (0.00, 0.59)	151	0.12 (-0.10, 0.33)	142	0.34 (-0.08, 0.76)
Quartile 3	159	-4.5 (-110.1, 101.0)	159	0.17 (-0.12, 0.46)	159	-0.02 (-0.23, 0.19)	152	-0.05 (-0.46, 0.37)
Quartile 4	139	-34.6 (-146.1, 76.9)	139	0.09 (-0.21, 0.40)	139	-0.09 (-0.31, 0.13)	136	0.00 (-0.44, 0.43)
Per IQR increase	588	-25.1 (-61.5, 11.4)	588	0.01 (-0.09, 0.11)	588	-0.05 (-0.13, 0.02)	565	-0.04 (-0.18, 0.10)

a – Models adjusted for maternal blood Pb and Mn (smoothed), maternal age at child's birth (smoothed), infant sex, race/ethnicity, parity, smoking during pregnancy, maternal education, prenatal vitamin use, and maternal hemoglobin at delivery.

b – Effect estimates represent change in birth outcomes for (1) arsenic quartiles 2, 3, 4 compared to quartile 1, or (2) IQR increase in arsenic (continuous $\log_e$-transformed concentrations, scaled to the IQR).

c – Maternal blood arsenic quartile 1: < 0.97 µg/l, quartile 2: ≥ 0.97 to < 1.4 µg/l, quartile 3: ≥ 1.4 to < 2.3 µg/l, quartile 4: ≥ 2.3 µg/l. d – Cord blood arsenic quartile 1: < 1.8 µg/l, quartile 2: ≥ 1.8 to < 2.4 µg/l, quartile 3: ≥ 2.4 to < 3.4 µg/l, quartile 4: ≥ 3.4 µg/l.

Table S2. Results from adjusted regression models[a] evaluating interactions of arsenic with lead and manganese[b].

Model and Exposure	Birth Weight (g)		Gestational Age (weeks)		Birth Weight for Gestational Age (z-score)		Head Circumference (cm)	
	n	Estimate (95% CI)	n	Estimate (95% CI)	n	Estimate (95% CI)	n	Estimate (95% CI)
Model 1	596		596		596		574	
Log_e Maternal As, per IQR increase[c]		-80.0 (-130.5, -29.6)		-0.13 (-0.27, 0.01)		-0.14 (-0.25, -0.04)		-0.23 (-0.43, -0.03)
Log_e Maternal Pb		41.1 (-35.2, 117.5)		0.14 (-0.07, 0.35)		0.05 (-0.10, 0.20)		0.37 (0.07, 0.67)
Maternal As * Pb		31.9 (-43.8, 107.6) p=0.41		-0.03 (-0.24, 0.18) p=0.79		0.07 (-0.08, 0.22) p=0.39		0.10 (-0.20, 0.39) p=0.52
Model 2	596		596		596		574	
Log_e Maternal As, per IQR increase		-79.0 (-131.2, -26.8)		-0.13 (-0.27, 0.02)		-0.14 (-0.25, -0.04)		-0.26 (-0.46, -0.05)
Log_e Maternal Mn		56.7 (-67.6, 180.9)		0.05 (-0.30, 0.39)		0.10 (-0.15, 0.35)		-0.61 (-1.1, -0.11)
Maternal As * Mn		12.9 (-102.2, 128.0) p=0.83		-0.03 (-0.35, 0.29) p=0.87		0.02 (-0.21, 0.25) p=0.85		0.24 (-0.21, 0.70) p=0.29
Model 3	588		588		588		565	
Log_e Cord As, per IQR increase[c]		-24.5 (-61.5, 12.4)		0.00 (-0.10, 0.10)		-0.05 (-0.13, 0.02)		-0.03 (-0.18, 0.11)
Log_e Cord Pb		31.6 (-76.0, 139.1)		0.16 (-0.14, 0.46)		0.02 (-0.19, 0.24)		0.27 (-0.15, 0.69)
Cord As * Pb		5.7 (-54.0, 65.4) p=0.85		-0.05 (-0.22, 0.11) p=0.54		0.02 (-0.10, 0.14) p=0.74		0.04 (-0.19, 0.27) p=0.72
Model 4	588		588		588		565	
Log_e Cord As, per IQR increase		-28.2 (-65.6, 9.2)		0.01 (-0.10, 0.11)		-0.06 (-0.13, 0.02)		-0.04 (-0.19, 0.10)

Log$_e$ Cord Mn		-146.7 (-324.8, 31.5)		-0.07 (-0.56, 0.42)		-0.31 (-0.67, 0.05)		-0.69 (-1.4, 0.01)
Cord As * Mn		39.0 (-61.5, 139.5) p=0.45		0.00 (-0.28, 0.28) p=0.99		0.09 (-0.11, 0.29) p=0.39		0.07 (-0.32, 0.46) p=0.74

a – Models adjusted for blood lead and manganese, mother's age at delivery, child sex, race/ethnicity, parity, smoking during pregnancy, maternal education, prenatal vitamin use, and maternal hemoglobin at delivery. Lead and manganese centered at mean of log$_e$ distribution.

b – One interaction term included in each model.

c – Continuous log$_e$-transformed arsenic concentrations, scaled to the IQR.

Table S3. Adjusted associations of maternal and cord blood arsenic with birth outcomes[a], with and without accounting for measurement error using inverse variance weighting

Exposure	Birth Weight (g)	Gestational Age (weeks)	Birth Weight for Gestational Age (z-score)	Head Circumference (cm)
	Estimate (95% CI)[b]	Estimate (95% CI)[b]	Estimate (95% CI)[b]	Estimate (95% CI)[b]
Log_e maternal As	-77.5 (-127.8, -27.3)	-0.13 (-0.27, 0.01)	-0.14 (-0.24, -0.04)	-0.22 (-0.42, -0.03)
Weighted log_e maternal As[c]	-77.1 (-126.7, -27.5)	-0.16 (-0.31, -0.02)	-0.13 (-0.23, -0.03)	-0.27 (-0.47, -0.08)
Log_e cord As	-25.1 (-61.5, 11.4)	0.01 (-0.09, 0.11)	-0.05 (-0.13, 0.02)	-0.04 (-0.18, 0.10)
Weighted log_e cord As[d]	-14.7 (-49.5, 20.1)	0.10 (0.01, 0.20)	-0.05 (-0.12, 0.02)	-0.01 (-0.12, 0.14)

a – Each line in table represents separate model. Models include blood lead and manganese, mother's age at delivery, child sex, race/ethnicity, parity, smoking during pregnancy, maternal education, prenatal vitamin use, and maternal hemoglobin at delivery.

b – Effect estimates represent change in birth outcomes per IQR increase in arsenic (continuous log_e-transformed concentrations, scaled to the IQR).

c – Weighted by the inverse of the variance of the maternal blood arsenic measurement.

d – Weighted by the inverse of the variance of the umbilical cord blood arsenic measurement.