

## Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

**eTable 1.** Baseline Characteristics of Children Included, Unavailable for Follow-up, and Excluded (N = 1152)

		Lost to follow-up or Excluded (n=782)		Included (n=370)		p-value
		n (%)		n (%)		
Geographic area	Central	485 (62.02)		267 (72.16)		< 0.01
	Eastern	297 (37.98)		103 (27.84)		
Sex	Boy	297 (50.94)		208 (56.22)		0.11
	Girl	286 (49.06)		162 (43.78)		
Maternal education (yrs)	≤ 12	95 (16.64)		47 (12.70)		0.01
	13–16	411 (71.98)		258 (69.73)		
	> 16	65 (11.38)		65 (17.57)		
Income per year (USD)	< 32420	359 (67.99)		173 (48.60)		< 0.01
	32420–47763	148 (28.03)		104 (29.21)		
	> 47763	21 (3.98)		79 (22.19)		
ETS exposure at pregnancy	Yes	256 (44.91)		130 (39.88)		0.14
	No	314 (55.09)		196 (60.12)		
Maternal allergies	Yes	135 (24.11)		172 (46.49)		< 0.01
	No	425 (75.89)		198 (53.51)		
		Mean ± SD		Mean ± SD		
Age		3.71 ± 0.64		3.94 ± 0.59		< 0.01
Birth weight (g)		3080 ± 449.3		3126 ± 383.4		0.11
Maternal age		31.52 ± 5.09		32.52 ± 4.04		< 0.01
Gestational weeks		38.41 ± 1.63		38.68 ± 1.14		0.04
		Median (IQR)	Mean ± SD	Median (IQR)	Mean ± SD	
Umaternal metal levels (µg·g cre <sup>-1</sup> )	As	50.27 (50.87)	69.93 ± 70.20	53.72 (53.03)	80.28 ± 108.7	0.07
	eΣiAs <sup>§</sup>	28.64 (7.37)	31.48 ± 10.17	29.14 (7.69)	32.98 ± 15.76	0.07
	Cd	0.80 (0.51)	0.98 ± 0.81	0.81 (0.64)	1.05 ± 1.02	0.32
	Pb	1.31 (0.85)	1.48 ± 1.10	1.35 (0.78)	1.90 ± 5.27	0.29
	Co	1.27 (1.00)	1.60 ± 1.33	1.33 (1.30)	1.61 ± 1.12	0.24
	Cu	18.63 (8.84)	20.77 ± 10.63	17.44 (7.48)	19.52 ± 11.83	< 0.01
	Ni	3.98 (4.00)	6.16 ± 11.90	3.95 (3.97)	6.67 ± 12.51	0.85
	Tl	0.31 (0.17)	0.33 ± 0.16	0.29 (0.16)	0.33 ± 0.22	0.56
	Zn	439.3 (337.2)	498.4 ± 311.4	453.6 (322.8)	528.4 ± 355.5	0.14

<sup>§</sup> eΣiAs (estimated total inorganic arsenic) = 21.35241 + 0.14493\*(As)

**eTable 2.** Spearman Correlation Coefficients for Total Arsenic, Total Inorganic Arsenic, and Estimated Total Inorganic Arsenic in Maternal Urine During Pregnancy in Previous TMICS Pilot Study With Arsenic Data Available (N = 336)

Species ( $\mu\text{g}\cdot\text{g}^{-1}$ )	As	$\Sigma\text{iAs}$	$\text{e}\Sigma\text{iAs}^{\S}$
As	1	0.61	1.00
		< 0.01	< 0.01
$\Sigma\text{iAs}$		1	0.61
			< 0.01
$\text{e}\Sigma\text{iAs}^{\S}$			1

$\Sigma\text{iAs}$  (total inorganic arsenic) = As(III) + As(V) + MMA + DMA

$\text{e}\Sigma\text{iAs}$  (estimated total inorganic arsenic) =  $21.35241 + 0.14493 \cdot (\text{As})$

The concentration of  $\Sigma\text{iAs}$  (median: 32.80; IQR: 22.50)

The concentration of  $\text{e}\Sigma\text{iAs}$  (median: 34.08; IQR: 13.68)

**eTable 3.** Characteristics of Children in Birth Cohort Classified by Geographic Area

		Central (n=267)		Eastern (n=103)		p-value
		n (%)		n (%)		
Sex	Boy	156 (58.43)		52 (50.49)		0.17
	Girl	111 (41.57)		51 (49.51)		
Maternal education (yrs)	≤ 12	29 (10.86)		18 (17.48)		0.15
	13–16	193 (72.28)		65 (63.11)		
	> 16	45 (16.85)		20 (19.42)		
Income per year (USD)	< 32420	115 (45.10)		58 (57.43)		0.01
	32420–47763	73 (28.63)		31 (30.69)		
	> 47763	67 (26.27)		12 (11.88)		
ETS exposure at pregnancy	Yes	88 (38.43)		42 (43.30)		0.46
	No	141 (61.57)		55 (56.70)		
ETS exposure at 4 yrs	Yes	47 (17.60)		29 (28.16)		0.02
	No	220 (82.40)		74 (71.84)		
Paternal allergies	Yes	93 (47.21)		32 (50.00)		0.70
	No	104 (52.79)		32 (50.00)		
Maternal allergies	Yes	127 (47.57)		45 (43.69)		0.50
	No	140 (52.43)		58 (56.31)		
Parental allergies	Yes	170 (63.67)		58 (56.31)		0.19
	No	97 (36.33)		45 (43.69)		
AD	Yes	79 (29.59)		31 (30.10)		0.92
		Mean ± SD		Mean ± SD		
Age		4.02 ± 0.61		3.74 ± 0.49		< 0.01
Birth weight (g)		3128 ± 383.0		3123 ± 386.6		0.92
Maternal age		32.62 ± 3.99		32.35 ± 4.15		0.61
Gestational weeks		38.46 ± 0.11		39.01 ± 1.11		< 0.01
		Median (IQR)	Mean ± SD	Median (IQR)	Mean ± SD	
U <sub>maternal</sub> metal levels (µg·g cre <sup>-1</sup> )	As	57.30 (51.28)	81.75 ± 119.7	48.94 (68.36)	76.47 ± 7.38	0.39
	eΣiAs <sup>§</sup>	29.66 (7.43)	33.20 ± 17.35	28.45 (9.91)	32.44 ± 10.63	0.39
	Cd	0.92 (0.71)	1.18 ± 1.13	0.61 (0.33)	0.71 ± 0.52	< 0.01
	Pb	1.44 (0.75)	1.87 ± 3.58	1.11 (0.67)	2.02 ± 8.19	< 0.01
	Co	1.37 (1.31)	1.63 ± 1.15	1.29 (1.24)	1.55 ± 1.05	0.50
	Cu	17.33 (6.96)	19.67 ± 12.21	18.33 (8.43)	19.14 ± 10.82	0.83
	Ni	4.09 (4.87)	7.68 ± 14.52	3.60 (3.08)	4.03 ± 2.49	0.03
	Tl	0.30 (0.16)	0.34 ± 0.24	0.29 (0.17)	0.31 ± 0.13	0.18
	Zn	468.5 (316.9)	554.2 ± 376.2	389.3 (307.7)	461.7 ± 286.5	< 0.01

<sup>§</sup> eΣiAs (estimated total inorganic arsenic) = 21.35241 + 0.14493\*(As)

**eTable 4.** Logistic Regression Analysis of Association Between Prenatal Exposure to Metals and Atopic Dermatitis in Children (N = 370)

	Model 1			Model 2		
U <sub>maternal metal levels (µg·g cre<sup>-1</sup>)</sub>	OR (95%CI)	p-value	q value	OR (95%CI)	p-value	q value
As	1.41 (1.15, 1.74)	< 0.01	0.01	1.49 (1.20, 1.85)	< 0.01	< 0.01
eΣiAs <sup>§</sup>	2.14 (1.23, 3.73)	0.01	0.02	2.36 (1.33, 4.19)	< 0.01	0.01
Cd	1.04 (0.80, 1.36)	0.74	0.98	1.02 (0.76, 1.36)	0.90	0.90
Pb	1.05 (0.80, 1.37)	0.74	0.97	1.06 (0.79, 1.41)	0.72	0.72
Co	0.99 (0.79, 1.25)	0.93	0.98	1.11 (0.83, 1.47)	0.49	0.51
Cu	1.01 (0.69, 1.45)	0.98	0.98	1.00 (0.67, 1.50)	0.99	0.99
Ni	0.91 (0.79, 1.06)	0.23	0.47	0.88 (0.74, 1.04)	0.14	0.21
Tl	1.03 (0.72, 1.48)	0.86	0.98	1.04 (0.70, 1.53)	0.86	0.86
Zn	0.94 (0.72, 1.24)	0.66	0.98	0.83 (0.62, 1.12)	0.23	0.28

Model 1: Adjustment for child's sex (boy or girl), geographic area (central or eastern) according to DAG

Model 2: Adjustment for propensity score for each exposure. It was calculated from child's sex (boy or girl), ETS exposure at 4 years of age (yes or no), maternal education (≤ 12 yrs, 13–16 yrs, > 16 yrs), parental allergies (yes or no), geographic area (central or eastern), exposure to other metals (the studied metal did not include)

<sup>§</sup> eΣiAs (estimated total inorganic arsenic) = 21.35241 + 0.14493\*(As)

The concentrations of metals were log<sub>2</sub>-transformed

**eTable 5.** Logistic Regression Analysis of Association Between Prenatal Exposure to Metals and Atopic Dermatitis in Children With Further Adjustment for Metals (N = 370)

	Model 1		Model 1		Model 2		Model 2	
<b>U<sub>maternal</sub> metal levels (µg·g cre<sup>-1</sup>)</b>	<b>OR (95%CI)</b>	<b>p-value</b>	<b>OR (95%CI)</b>	<b>p-value</b>	<b>OR (95%CI)</b>	<b>p-value</b>	<b>OR (95%CI)</b>	<b>p-value</b>
As	1.48 (1.19, 1.84)	< 0.01	—		1.47 (1.18, 1.84)	< 0.01	—	
eΣiAs <sup>§</sup>	—		2.34 (1.31, 4.19)	< 0.01	—		2.28 (1.27, 4.09)	0.01
Cd	1.01 (0.74, 1.37)	0.97	1.02 (0.75, 1.39)	0.89	1.02 (0.75, 1.40)	0.90	1.03 (0.76, 1.41)	0.83
Pb	1.01 (0.74, 1.39)	0.94	1.03 (0.75, 1.40)	0.88	1.03 (0.74, 1.43)	0.86	1.04 (0.76, 1.44)	0.79
Co	1.07 (0.81, 1.43)	0.62	1.08 (0.81, 1.43)	0.60	1.07 (0.80, 1.43)	0.63	1.08 (0.81, 1.44)	0.61
Cu	1.06 (0.68, 1.66)	0.78	1.06 (0.68, 1.64)	0.21	1.12 (0.71, 1.78)	0.62	1.12 (0.71, 1.77)	0.62
Ni	0.87 (0.73, 1.04)	0.12	0.87 (0.73, 1.03)	0.11	0.86 (0.72, 1.03)	0.10	0.86 (0.72, 1.03)	0.10
Tl	0.92 (0.61, 1.40)	0.70	0.94 (0.62, 1.42)	0.77	0.87 (0.56, 1.34)	0.52	0.89 (0.58, 1.36)	0.58
Zn	0.84 (0.62, 1.14)	0.26	0.87 (0.64, 1.17)	0.35	0.80 (0.58, 1.10)	0.17	0.83 (0.60, 1.13)	0.23

<sup>§</sup> eΣiAs (estimated total inorganic arsenic) = 21.35241 + 0.14493\*(As)

Model 1: Adjustment for child's sex (boy or girl), geographic area (central or eastern) according to DAG; all metals in the model

Model 2: Adjustment for child's sex (boy or girl), parental allergies (yes or no), geographic area (central or eastern), ETS exposure at 4 years of age (yes or no); all metals in the model

The concentrations of metals were log<sub>2</sub>-transformed

**eTable 6.** Logistic Regression Analysis of Association Between Prenatal Exposure to Metals and Atopic Dermatitis in Children Without Categorization by Creatinine Urinary Levels (N = 370)

U <sub>maternal</sub> metal levels (µg/L)	Model 1			Model 2		
	OR (95%CI)	p-value	q value	OR (95%CI)	p-value	q value
As	1.32 (1.12, 1.56)	< 0.01	0.01	1.32 (1.11, 1.57)	< 0.01	0.01
eΣiAs <sup>§</sup>	2.25 (1.25, 4.05)	0.01	0.03	2.22 (1.23, 4.02)	0.01	0.04
Cd	1.08 (0.91, 1.30)	0.38	0.63	1.10 (0.91, 1.32)	0.32	0.55
Pb	1.12 (0.91, 1.38)	0.30	0.63	1.14 (0.92, 1.41)	0.24	0.55
Co	1.06 (0.88, 1.27)	0.54	0.63	1.07 (0.89, 1.29)	0.50	0.64
Cu	1.08 (0.88, 1.31)	0.46	0.63	1.09 (0.90, 1.34)	0.36	0.55
Ni	0.96 (0.84, 1.10)	0.56	0.63	0.97 (0.84, 1.10)	0.60	0.67
Tl	1.11 (0.89, 1.38)	0.36	0.63	1.11 (0.89, 1.39)	0.37	0.55
Zn	1.04 (0.86, 1.25)	0.69	0.69	1.04 (0.86, 1.26)	0.71	0.71

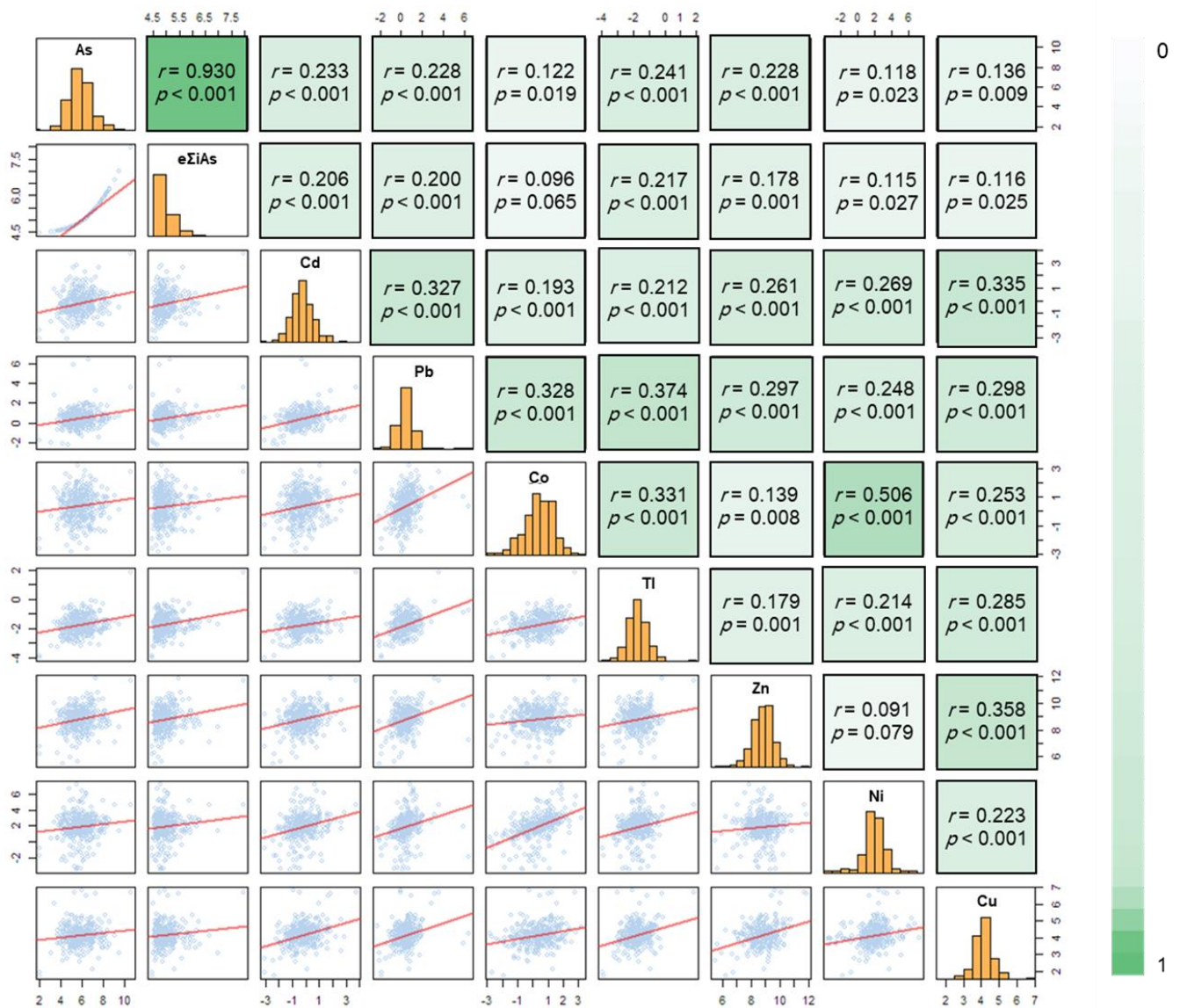
<sup>§</sup> eΣiAs (estimated total inorganic arsenic) = 15.065 + 0.122\*(As)

Model 1: Adjustment for child's sex (boy or girl), geographic area (central or eastern) according to DAG; U<sub>maternal</sub> metal levels without urinary creatinine correction

Model 2: Adjustment for child's sex (boy or girl), parental allergies (yes or no), geographic area (central or eastern), ETS exposure at 4 years of age (yes or no); U<sub>maternal</sub> metal levels without urinary creatinine correction

The concentrations of metals were log<sub>2</sub>-transformed

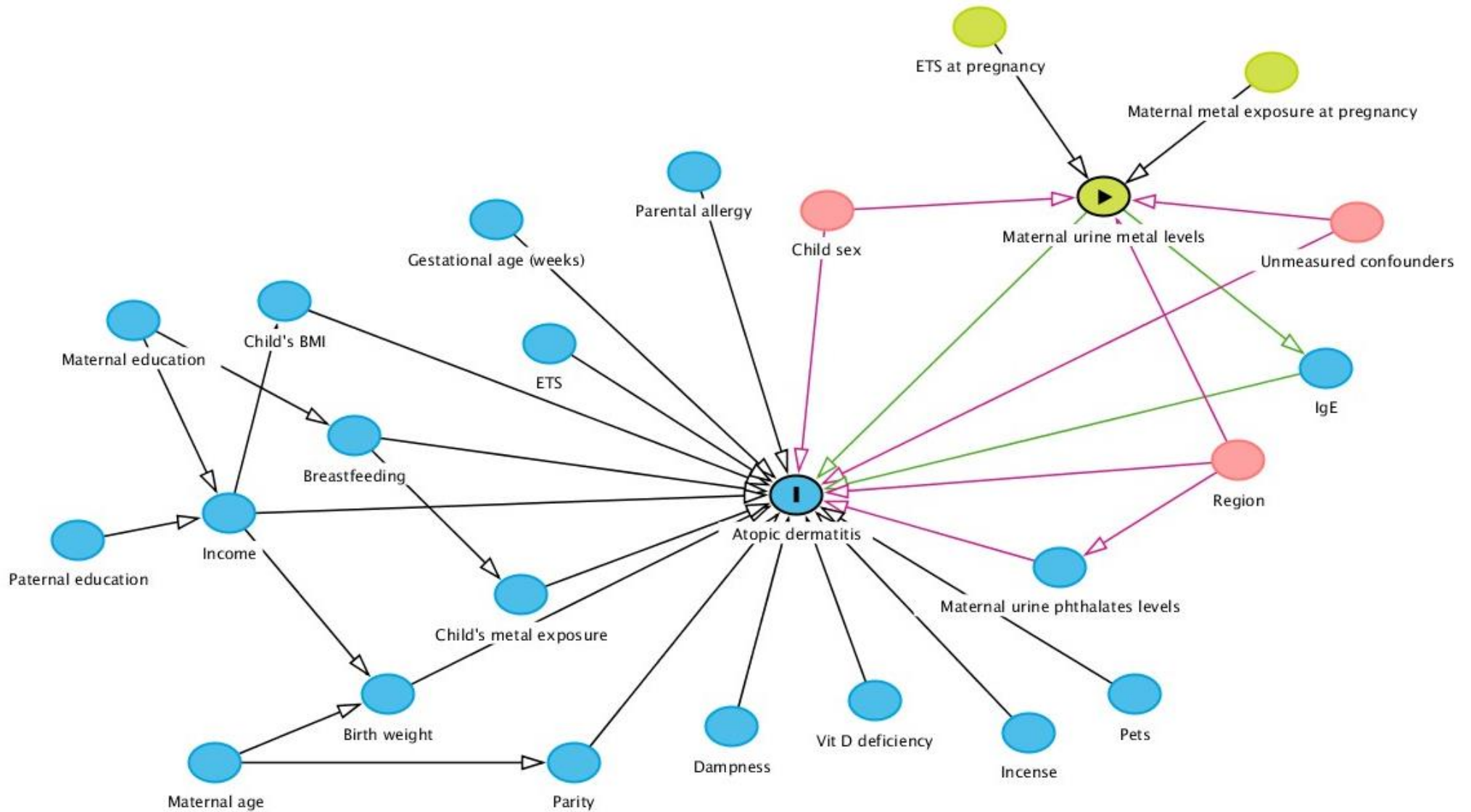
**eFigure 1.** Correlation Matrix of Maternal Urinary Metal Concentrations



Metal concentrations measured by  $\mu\text{g}\cdot\text{g cre}^{-1}$ .  $e\Sigma\text{iAs}$  (estimated total inorganic arsenic) =  $21.35241 + 0.14493^*(\text{As})$ . The concentrations of metals were  $\log_2$ -transformed for normality.



**eFigure 2.** Directed Acyclic Graph of Confounding Variables



Red oval: confounding factor; blue oval: other factors; green oval: ancestor of exposure; green oval with solid triangle: exposure; blue oval with vertical bar: outcome.