Supplemental Material

Trimester-Specific Blood Trihalomethane and Urinary Haloacetic Acid Concentrations and Adverse Birth Outcomes: Identifying Windows of Vulnerability during Pregnancy

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Table S1. Sensitivity analysis for associations between blood trihalomethane and urinary haloacetic acid concentrations (tertiles or categories) and risk of small for gestational age by pregnancy trimesters, excluding women reporting occupational exposures to organic/chlorinated solvents.[a]							
Biomarkers	First trimester		Second trimester		Third trimester		Type 3 P-Value[c]
	RR (95% CI)	n/N	RR (95% CI)	n/N	RR (95% CI)	n/N	
THMs							
TCM							0.08
T1 (1.34-7.45 ng/L)	1.0	24/425	1.0	8/341	1.0	8/293	
T2 (7.46-13.46 ng/L)	0.75 (0.40, 1.40)	18/422	2.37 (1.04 5.43)	19/340	2.50 (1.10, 5.69)	21/279	
T3 (>13.46 ng/L)	0.95 (0.53, 1.72)	21/410	2.38 (1.05, 5.41)	22/350	2.12 (0.91, 4.94)	17/287	
P-trend	0.85		0.047		0.10		
BDCM							0.14
T1 (0.35-0.65 ng/L)	1.0	27/433	1.0	20/347	1.0	19/285	
T2 (0.66-1.00 ng/L)	0.86 (0.48, 1.52)	22/417	0.83 (0.43, 1.61)	17/350	0.64(0.31, 1.31)	13/287	
T3 (>1.00 ng/L)	0.58 (0.30, 1.11)	14/408	0.63 (0.31, 1.30)	12/334	0.74 (0.37, 1.49)	14/287	
P-trend	0.10		0.21		0.37		
DBCM							0.39
<60th (0.50-0.75 ng/L)	1.0	31/765	1.0	31/621	1.0	28/531	
60-80th (0.76-1.20 ng/L)	1.81(0.99, 3.29)	17/247	0.79 (0.36, 1.72)	8/200	0.92 (0.42, 2.03)	9/162	
>80th (>1.20 ng/L)	1.56 (0.84, 2.89)	15/245	0.92 (0.45, 1.90)	10/210	1.07 (0.50, 2.29)	9/166	
P-trend	0.09		0.72		0.91		
TBM							0.77
<60th (1.41-3.77 ng/L)	1.0	36/750	1.0	30/624	1.0	27/518	
60-80th (3.78-14.44 ng/L)	1.17 (0.63, 2.19)	14/254	1.18 (0.59, 2.37)	11/201	1.01 (0.47, 2.16)	9/170	
>80th (>14.44 ng/L)	1.08 (0.57, 2.04)	13/253	0.77 (0.35, 1.70)	8/206	1.19 (0.57, 2.49)	10/171	
P-trend	0.74		0.65		0.67		
Br-THMs							0.64
T1 (2.26-3.00 ng/L)	1.0	19/436	1.0	20/339	1.0	14/299	
T2 (3.01-7.76 ng/L)	1.29 (0.69, 2.43)	21/404	0.76 (0.38, 1.52)	14/345	1.28 (0.62, 2.64)	17/273	
T3 (>7.76 ng/L)	1.32(0.71, 2.45)	23/417	0.75 (0.36, 1.48)	15/347	1.14 (0.55, 2.36)	15/287	
P-trend	0.39		0.39		0.73		
TTHMs							0.95

T1 (3.60-12.80 ng/L)	1.0	21/433	1.0	12/339	1.0	15/283	
T2 (12.81-23.68 ng/L)	1.21 (0.68, 2.18)	25/403	1.52 (0.73, 3.15)	20/348	1.02 (0.49, 2.13)	15/290	
T3 (>23.68 ng/L)	0.84 (0.44, 1.60)	17/421	1.31(0.62, 2.76)	17/344	1.15(0.56, 2.37)	16/286	
P-trend	0.63		0.51		0.71		
HAAs[b]							
TCAA							0.70
T1 (0.35-1.17 µg/L)	1.0	17/388	1.0	17/345	1.0	13/296	
T2 (1.18-2.23 µg/L)	1.61 (0.81, 3.21)	25/367	1.12 (0.55, 2.28)	19/336	1.56 (0.74, 3.27)	21/274	
T3 (>2.23 µg/L)	1.32 (0.54, 3.24)	16/382	0.94 (0.43, 2.07)	15/350	1.03 (0.46, 2.33)	14/284	
P-trend	0.50		0.87		0.99		
DCAA							0.97
T1 (0.71-5.14 µg/L)	1.0	17/385	1.0	18/352	1.0	18/296	
T2 (5.15-8.90 µg/L)	1.58 (0.81, 3.09)	25/367	0.89 (0.44, 1.79)	16/338	1.08 (0.54, 2.19)	18/276	
T3 (>8.90 µg/L)	1.23 (0.50, 3.03)	16/385	0.93 (0.42, 2.07)	17/341	0.65 (0.30, 1.42)	12/282	
P-trend	0.54		0.85		0.28		

Abbreviations: TCM, chloroform; BDCM, bromodichloromethane; DBCM, dibromochloromethane; TBM, bromoform; DCAA, dichloroacetic acid; TCAA, trichloroacetic acid; Br-THM, brominated trihalomethanes; TTHMs, total trihalomethanes; THMs, trihalomethanes; HAAs, haloacetic acids; n, numerator for cases of study outcome; N, total number of participants per subgroup. First trimester: gestational age <14 weeks; mean, 9.2±2.3 weeks. Second trimester: gestational age 14-27 weeks; mean, 17.1±2.0 weeks. Third trimester: gestational age >27 weeks; mean 31.8±2.3 weeks). [a]Adjusted for maternal age, body mass index at recruitment, household income, active/passive smoking status, gestational age at sampling, the time of day of sample collection, infant sex, and delivery model. [b] Models were additionally adjusted for creatinine by including the concentrations as continuous covariates. [c]Type 3 tests were conducted based on multiple informant models by fitting generalized estimating equations with a log link function and Poisson distribution; a Type 3 p-value of <0.10 indicated that the associations differed significantly across pregnancy trimesters.

Table S2. Sensitivity analysis for associations between blood trihalomethane and urinary haloacetic acid concentrations (tertiles or categories) and risk of small for gestational age by pregnancy trimesters, with adjustment for both pre-pregnancy BMI and trimester-specific weight gain.[a]

Biomarkers	First trimester		Second trimester		Third trimester		Type 3 P-Value[c]
	RR (95% CI)	n/N	RR (95% CI)	n/N	RR (95% CI)	n/N	
THMs							
TCM							0.06
T1 (1.34-7.45 ng/L)	1.0	24/425	1.0	8/341	1.0	8/293	
T2 (7.46-13.46 ng/L)	0.80 (0.43, 1.48)	18/422	2.33 (1.02 5.33)	19/340	2.62 (1.15, 5.94)	21/279	
T3 (>13.46 ng/L)	0.94 (0.52, 1.69)	21/410	2.44 (1.08, 5.52)	22/350	2.09 (0.90, 4.86)	17/287	
P-trend	0.81		0.04		0.12		
BDCM							0.12
T1 (0.35-0.65 ng/L)	1.0	27/433	1.0	20/347	1.0	19/285	
T2 (0.66-1.00 ng/L)	0.84 (0.48, 1.48)	22/417	0.89 (0.47, 1.71)	17/350	0.69(0.34, 1.40)	13/287	
T3 (>1.00 ng/L)	0.57 (0.30, 1.08)	14/408	0.62 (0.30, 1.27)	12/334	0.73 (0.36, 1.48)	14/287	
P-trend	0.09		0.20		0.37		
DBCM							0.45
<60th (0.50-0.75 ng/L)	1.0	31/765	1.0	31/621	1.0	28/531	
60-80th (0.76-1.20 ng/L)	1.74(0.96, 3.16)	17/247	0.76 (0.35, 1.66)	8/200	1.00 (0.47, 2.13)	9/162	
>80th (>1.20 ng/L)	1.50 (0.81, 2.79)	15/245	0.89 (0.43, 1.82)	10/210	1.08 (0.50, 2.29)	9/166	
P-trend	0.11		0.64		0.87		
TBM							0.73
<60th (1.41-3.77 ng/L)	1.0	36/750	1.0	30/624	1.0	27/518	
60-80th (3.78-14.44 ng/L)	1.18 (0.64, 2.20)	14/254	1.13 (0.56, 2.26)	11/201	1.01 (0.47, 2.16)	9/170	
>80th (>14.44 ng/L)	1.07 (0.57, 2.032)	13/253	0.76 (0.35, 1.66)	8/206	1.17 (0.56, 2.43)	10/171	
P-trend	0.74		0.59		0.70		
Br-THMs							0.57
T1 (2.26-3.00 ng/L)	1.0	19/436	1.0	20/339	1.0	14/299	
T2 (3.01-7.76 ng/L)	1.23 (0.66, 2.30)	21/404	0.73 (0.37, 1.45)	14/345	1.31 (0.64, 2.69)	17/273	
T3 (>7.76 ng/L)	1.29(0.70, 2.37)	23/417	0.72 (0.36, 1.40)	15/347	1.15 (0.55, 2.38)	15/287	
P-trend	0.42		0.32		0.71		

	First trimester		Second trimester		Third trimester		Type 3 p-value[c]
	OR (95% CI)[a]	n/N	OR (95% CI)[a]	n/N	OR (95% CI)[a]	n/N	
TTHMs							0.96
T1 (3.60-12.80 ng/L)	1.0	21/433	1.0	12/339	1.0	15/283	
T2 (12.81-23.68 ng/L)	1.28 (0.71, 2.28)	25/403	1.54 (0.75, 3.18)	20/348	0.96 (0.47, 1.97)	15/290	
T3 (>23.68 ng/L)	0.85 (0.45, 1.61)	17/421	1.29(0.61, 2.72)	17/344	1.08(0.53, 2.19)	16/286	
P-trend	0.65		0.54		0.84		
HAAs[b]							
TCAA							0.69
T1 (0.35-1.17 μg/L)	1.0	17/388	1.0	17/345	1.0	13/296	
T2 (1.18-2.23 μg/L)	1.67 (0.84, 3.30)	25/367	1.17 (0.58, 2.35)	19/336	1.64 (0.78, 3.42)	21/274	
T3 (>2.23 μg/L)	1.26 (0.51, 3.08)	16/382	0.93 (0.43, 2.04)	15/350	1.04 (0.46, 2.36)	14/284	
P-trend	0.56		0.84		0.99		
DCAA							0.92
T1 (0.71-5.14 μg/L)	1.0	17/385	1.0	18/352	1.0	18/296	
T2 (5.15-8.90 μg/L)	1.68 (0.87, 3.25)	25/367	0.90 (0.45, 1.82)	16/338	1.03 (0.51, 2.07)	18/276	
T3 (>8.90 μg/L)	1.18 (0.48, 2.89)	16/385	1.01 (0.46, 2.21)	17/341	0.60 (0.28, 1.29)	12/282	
P-trend	0.58		0.98		0.19		

Abbreviations: TCM, chloroform; BDCM, bromodichloromethane; DBCM, dibromochloromethane; TBM, bromoform; DCAA, dichloroacetic acid; TCAA, trichloroacetic acid; Br-THM, brominated trihalomethanes; TTHMs, total trihalomethanes; THMs, trihalomethanes; HAAs, haloacetic acids; n, numerator for cases of study outcome; N, total number of participants per subgroup. First trimester: gestational age <14 weeks; mean, 9.2±2.3 weeks. Second trimester: gestational age 14-27 weeks; mean, 17.1±2.0 weeks. Third trimester: gestational age >27 weeks; mean 31.8±2.3 weeks). [a]Adjusted for maternal age, body mass index at recruitment, household income, trimester-specific weight gain, active/passive smoking status, gestational age at sampling, the time of day of sample collection, infant sex, and delivery model. [b]Models were additionally adjusted for creatinine by including the concentrations as continuous covariates. [c]Type 3 tests were conducted based on multiple informant models by fitting generalized estimating equations with a log link function and Poisson distribution; a Type 3 p-value of <0.10 indicated that the associations differed significantly across pregnancy trimesters.

Biomarkers	First trimester		Second trimester		Third trimester		Type 3 P-Value
	RR (95% CI)	n/N	RR (95% CI)	n/N	RR (95% CI)	n/N	

Table S3. Associations between blood trihalomethane and urinary haloacetic acid concentrations (tertiles or categories) and risk of low birthweight by pregnancy trimesters.

Biomarkers	RR (95% CI)	n/N	RR (95% CI)	n/N	RR (95% CI)	n/N	Type 3 P-Value
THMs							
TCM							0.67
T1 (1.34-7.45 ng/L)	1.0	9/510	1.0	6/412	1.0	7/340	
T2 (7.46-13.46 ng/L)	1.47 (0.63, 3.44)	13/496	1.58(0.56, 4.46)	9/409	1.73 (0.67, 4.50)	11/336	
T3 (>13.46 ng/L)	1.41 (0.59, 3.35)	12/497	2.20 (0.83, 5.82)	13/405	1.16 (0.42, 3.20)	8/339	
P-trend	0.45		0.11		0.79		
BDCM							0.88
T1 (0.35-0.65 ng/L)	1.0	13/507	1.0	7/419	1.0	10/337	
T2 (0.66-1.00 ng/L)	0.98 (0.45, 2.16)	12/497	1.88 (0.75, 4.71)	13/401	1.01 (0.42, 2.43)	10/334	
T3 (>1.00 ng/L)	0.72 (0.31, 1.70)	9/499	1.22 (0.44, 3.39)	8/406	0.59 (0.21, 1.62)	6/344	
P-trend	0.47		0.70		0.31		
DBCM							0.97
<60th (0.50-0.75 ng/L)	1.0	18/908	1.0	18/745	1.0	16/614	
60-80th (0.76-1.20 ng/L)	1.94 (0.93, 4.04)	12/298	0.85 (0.31, 2,28)	5/238	0.60 (0.18, 2.08)	3/200	
>80th (>1.20 ng/L)	0.68 (0.23, 2.02)	4/297	0.84 (0.31, 2.28)	5/243	1.27 (0.52, 3.08)	7/201	
P-trend	0.95		0.69		0.77		
TBM							0.66
<60th (1.41-3.77 ng/L)	1.0	19/900	1.0	18/742	1.0	14/611	
60-80th (3.78-14.44 ng/L)	1.47 (0.66, 3.27)	9/298	1.03 (0.41, 2.60)	6/244	1.03 (0.37, 2.88)	5/199	
>80th (>14.44 ng/L)	0.96 (0.38, 2.41)	6/305	0.68 (0.23, 2.04)	4/240	1.33 (0.53, 3.34)	7/205	
P-trend	0.86		0.55		0.56		
Br-THMs							0.77
T1 (2.26-3.00 ng/L)	1.0	10/506	1.0	7/418	1.0	7/348	
T2 (3.01-7.76 ng/L)	1.38 (0.60, 3.16)	13/494	1.92 (0.77, 4.83)	13/399	1.61 (0.61,4.23)	10/327	
T3 (>7.76 ng/L)	1.17 (0.50, 2.76)	11/503	1.18 (0.43, 3.28)	8/409	1.22 (0.45, 3.31)	9/340	
P-trend	0.72		0.75		0.71		

TTHMs							0.92
T1 (3.60-12.80 ng/L)	1.0	11/510	1.0	8/410	1.0	9/336	
T2 (12.81-23.68 ng/L)	1.04(0.45, 2.40)	11/491	1.68 (0.69, 4.11)	13/408	0.93 (0.36, 2.42)	8/341	
T3 (>23.68 ng/L)	1.16 (0.51, 2.62)	12/502	0.90 (0.32, 2.50)	7/408	0.92 (0.36, 2.34)	9/338	
P-trend	0.73		0.86		0.86		
HAAs[b]							
TCAA							0.07
T1 (0.35-1.17 µg/L)	1.0	16/456	1.0	11/409	1.0	7/345	
T2 (1.18-2.23 µg/L)	0.63 (0.26, 1.53)	10/459	1.15 (0.47, 2.83)	11/408	0.92 (0.32, 2.66)	9/336	
T3 (>2.23 µg/L)	0.43 (0.12, 1.48)	6/454	0.94 (0.34, 2.64)	8/412	1.00 (0.37, 2.75)	10/332	
P-trend	0.16		0.92		0.97		
DCAA							0.27
T1 (0.71-5.14 µg/L)	1.0	14/460	1.0	10/415	1.0	7/345	
T2 (5.15-8.90 µg/L)	0.88 (0.37, 2.05)	11/452	1.49 (0.63, 3.52)	13/406	0.89 (0.30, 2.63)	8/340	
T3 (>8.90 µg/L)	0.81 (0.24, 2.70)	7/457	0.94 (0.31, 2.86)	7/408	1.19(0.44, 3.19)	11/328	
P-trend	0.71		0.98		0.68		

Abbreviations: TCM, chloroform; BDCM, bromodichloromethane; DBCM, dibromochloromethane; TBM, bromoform; DCAA, dichloroacetic acid; TCAA, trichloroacetic acid; Br-THM, brominated trihalomethanes; TTHMs, total trihalomethanes; THMs, trihalomethanes; HAAs, haloacetic acids; n, numerator for cases of study outcome; N, total number of participants per subgroup. First trimester: gestational age <14 weeks; mean, 9.2±2.3 weeks. Second trimester: gestational age 14-27 weeks; mean, 17.1±2.0 weeks. Third trimester: gestational age >27 weeks; mean 31.8±2.3 weeks). [a]Adjusted for maternal age, body mass index at recruitment, household income, active/passive smoking status, gestational age at sampling, the time of day of sample collection, infant sex, and delivery mode. [b]Models were additionally adjusted for creatinine by including the concentrations as continuous covariates. [c]Type 3 tests were conducted based on multiple informant models by fitting generalized estimating equations with a log link function and Poisson distribution; a Type 3 p-value of <0.10 indicated that the associations differed significantly across pregnancy trimesters.

Table S4. Associations between blood trihalomethane and urinary haloacetic acid concentrations (tertiles or categories) and risk of preterm birth by pregnancy trimesters.							
Biomarkers	First trimester		Second trimester		Third trimester		Type 3 P-Value
	RR (95% CI)	n/N	RR (95% CI)	n/N	RR (95% CI)	n/N	
THMs							
TCM							0.63
T1 (1.34-7.45 ng/L)	1.0	21/524	1.0	14/431	1.0	16/355	
T2 (7.46-13.46 ng/L)	1.05 (0.58, 1.91)	23/523	1.23 (0.60, 2.49)	17/429	0.72 (0.33, 1.55)	11/361	
T3 (>13.46 ng/L)	0.67 (0.34, 1.32)	14/531	1.27 (0.62, 2.58)	17/429	0.75 (0.35, 1.58)	12/358	
P-trend	0.27		0.52		0.43		
BDCM							0.45
T1 (0.35-0.65 ng/L)	1.0	24/522	1.0	12/441	1.0	10/360	
T2 (0.66-1.00 ng/L)	0.60 (0.31, 1.16)	14/529	1.52 (0.73, 3.15)	18/424	1.25 (0.55, 2.88)	13/359	
T3 (>1.00 ng/L)	0.85 (0.47, 1.55)	20/527	1.63(0.78, 3.40)	18/424	1.55 (0.70, 3.44)	16/355	
P-trend	0.58		0.20		0.28		
DBCM							0.37
<60th (0.50-0.75 ng/L)	1.0	34/948	1.0	35/769	1.0	25/648	
60-80th (0.76-1.20 ng/L)	1.21(0.65, 2.26)	14/316	0.61 (0.27, 1.38)	7/256	0.60 (0.23, 1.56)	5/217	
>80th (>1.20 ng/L)	0.89 (0.44, 1.80)	10/314	0.54 (0.23, 1.30)	6/264	1.05 (0.49, 2.26)	9/209	
P-trend	0.89		0.11		0.88		
TBM							0.65
<60th (1.41-3.77 ng/L)	1.0	37/945	1.0	33/778	1.0	24/643	
60-80th (3.78-14.44 ng/L)	0.78 (0.39, 1.58)	10/317	0.54 (0.23, 1.30)	6/257	0.58 (0.22, 1.52)	5/217	
>80th (>14.44 ng/L)	0.89 (0.45, 1.74)	11/316	0.85 (0.40, 1.79)	9/254	1.12 (0.53, 2.37)	10/214	
P-trend	0.61		0.44		0.97		
Br-THMs							0.97
T1 (2.26-3.00 ng/L)	1.0	19/530	1.0	16/433	1.0	11/363	
T2 (3.01-7.76 ng/L)	1.23 (0.66, 2.28)	22/520	1.17 (0.60, 2.28)	19/427	1.38 (0.63, 3.01)	15/353	
T3 (>7.76 ng/L)	0.89 (0.46, 1.72)	17/528	0.83 (0.40, 1.73)	13/429	1.08 (0.48, 2.43)	13/358	

	Trimester 1 OR (95% CI)	n/N	Trimester 2 OR (95% CI)	n/N	Trimester 3 OR (95% CI)	n/N	Type 3 p-value[c]
P-trend	0.74		0.64		0. 87		
TTHMs							0.38
T1 (3.60-12.80 ng/L)	1.0	25/520	1.0	16/427	1.0	17/356	
T2 (12.81-23.68 ng/L)	0.70 (0.38, 1.30)	17/527	1.17 (0.60, 2.31)	18/431	0.48 (0.21, 1.12)	8/363	
T3 (>23.68 ng/L)	0.65 (0.35, 1.22)	16/531	0.92 (0.45, 1.90)	14/431	0.76 (0.37, 1.54)	14/355	
P-trend	0.17		0.84		0.42		
HAAs[b]							
TCAA							0.58
T1 (0.35-1.17 µg/L)	1.0	21/435	1.0	18/381	1.0	12/331	
T2 (1.18-2.23 µg/L)	0.70 (0.33, 1.48)	15/439	0.73 (0.35, 1.51)	15/401	0.77 (0.32, 1.83)	10/323	
T3 (>2.23 µg/L)	1.09 (0.46, 2.59)	19/433	0.74 (0.34, 1.57)	16/386	1.32 (0.57, 3.04)	17/321	
P-trend	0.86		0.44		0.46		
DCAA							0.64
T1 (0.71-5.14 µg/L)	1.0	19/437	1.0	16/395	1.0	13/330	
T2 (5.15-8.90 µg/L)	0.97 (0.49, 1.93)	18/441	1.14 (0.58, 2.23)	20/383	0.94 (0.43, 2.06)	14/320	
T3 (>8.90 µg/L)	1.07 (0.45, 2.53)	18/429	0.63 (0.28, 1.42)	13/390	0.72 (0.31, 1.68)	12/325	
P-trend	0.90		0.29		0.44		

Abbreviations: TCM, chloroform; BDCM, bromodichloromethane; DBCM, dibromochloromethane; TBM, bromoform; DCAA, dichloroacetic acid; TCAA, trichloroacetic acid; Br-THM, brominated trihalomethanes; TTHMs, total trihalomethanes; THMs, trihalomethanes; HAAs, haloacetic acids; n, numerator for cases of study outcome; N, total number of participants per subgroup. First trimester: gestational age <14 weeks; mean, 9.2±2.3 weeks. Second trimester: gestational age 14-27 weeks; mean, 17.1±2.0 weeks. Third trimester: gestational age >27 weeks; mean 31.8±2.3 weeks). [a]Adjusted for maternal age, body mass index at recruitment, household income, active/passive smoking status, gestational age at sampling, the time of day of sample collection, infant sex, and delivery model. [b]Models were additionally adjusted for creatinine by including the concentrations as continuous covariates. [c]Type 3 tests were conducted based on multiple informant models by fitting generalized estimating equations with a log link function and Poisson distribution; a Type 3 p-value of <0.10 indicated that the associations differed significantly across pregnancy trimesters.

Table S5. Sensitivity analysis for associations between urinary haloacetic acid concentrations (tertiles or categories) and risk of small for gestational age, low birthweight, and preterm birth, restricting the analysis among women who had a normal range of urinary creatinine (i.e., >0.3 to <3 g/L). [a]

Biomarkers	First trimester		Second trimester		Third trimester		Type 3 P-Value[b]
	RR (95% CI)	n/N	RR (95% CI)	n/N	RR (95% CI)	n/N	
Small for gestational age							
TCAA							0.77
T1(0.35-1.17 µg/L)	1.0	5/114	1.0	12/262	1.0	11/213	
T2(1.18-2.23 µg/L)	1.56 (0.56, 4.32)	20/326	1.33 (0.62, 2.83)	19/342	1.53 (0.69, 3.40)	19/277	
T3(>2.23 µg/L)	1.37 (0.42, 4.39)	14/371	1.01 (0.44, 2.33)	14/353	1.16 (0.46, 2.93)	14/289	
P-trend	0.72		0.97		0.80		
DCAA							0.86
T1(0.71-5.14 µg/L)	1.0	6/124	1.0	13/268	1.0	15/208	
T2(5.15-8.90 µg/L)	1.50 (0.55, 4.11)	20/311	0.93 (0.44, 1.96)	16/346	0.93(0.45, 1.91)	17/284	
T3(>8.90 µg/L)	1.03 (0.33, 3.21)	13/376	1.10 (0.48, 2.53)	16/343	0.57 (0.24, 1.38)	12/287	
P-trend	0.88		0.82		0.22		
Low birthweight							
TCAA							0.24
T1(0.35-1.17 µg/L)	1.0	2/130	1.0	9/310	1.0	7/241	
T2(1.18-2.23 µg/L)	1.12(0.23, 5.44)	8/387	1.05 (0.42, 2.63)	11/404	0.72(0.25, 2.07)	8/327	
T3(>2.23 µg/L)	0.65(0.11, 3.83)	6/429	0.86 (0.30, 2.44)	8/407	0.65 (0.20, 2.11)	9/333	
P-trend	0.48		0.77		0.48		
DCAA							0.75
T1(0.71-5.14 µg/L)	1.0	3/143	1.0	8/312	1.0	7/234	
T2(5.15-8.90 µg/L)	0.73(0.18, 2.89)	7/368	1.35 (0.55, 3.29)	13/410	0.69 (0.24, 2.01)	7/335	
T3(>8.90 µg/L)	0.50 (0.11, 2.26)	6/435	0.88 (0.29, 2.71)	7/399	0.84(0.27, 2.57)	10/332	
P-trend	0.36		0.88		0.76		

Preterm birth							
TCAA							0.94
T1(0.35-1.17 µg/L)	1.0	7/133	1.0	14/331	1.0	9/255	
T2(1.18-2.23 µg/L)	0.54 (0.21, 1.42)	13/412	0.72 (0.34, 1.53)	15/430	0.83 (0.33, 2.08)	10/350	
T3(>2.23 µg/L)	0.89 (0.32, 2.45)	19/466	0.67 (0.30, 1.49)	15/434	1.49 (0.58, 3.87)	16/357	
P-trend	0.84		0.34		0.36		
DCAA							0.76
T1(0.71-5.14 µg/L)	1.0	6/149	1.0	12/331	1.0	10/245	
T2(5.15-8.90 µg/L)	0.84 (0.32, 2.19)	15/395	1.21(0.59, 2.49)	20/433	0.90 (0.39, 2.05)	14/354	
T3(>8.90 µg/L)	0.89 (0.33, 2.41)	18/467	0.62 (0.26, 1.45)	12/431	0.61 (0.23, 1.62)	11/363	
P-trend	0.86		0.27		0.32		

Abbreviations: TCM, chloroform; BDCM, bromodichloromethane; DBCM, dibromochloromethane; TBM, bromoform; DCAA, dichloroacetic acid; TCAA, trichloroacetic acid; Br-THM, brominated trihalomethanes; TTHMs, total trihalomethanes; THMs, trihalomethanes; HAAs, haloacetic acids; n, numerator for cases of study outcome; N, total number of participants per subgroup. First trimester: gestational age <14 weeks; mean, 9.2±2.3 weeks. Second trimester: gestational age 14-27 weeks; mean, 17.1±2.0 weeks. Third trimester: gestational age >27 weeks; mean 31.8±2.3 weeks). [a]Adjusted for maternal age, body mass index at recruitment, household income, active/passive smoking status, gestational age at sampling, the time of day of sample collection, infant sex, delivery model, and urinary creatinine (including as a continuous covariates). [b]Type 3 tests were conducted based on multiple informant models by fitting generalized estimating equations with a log link function and Poisson distribution; a Type 3 p-value of <0.10 indicated that the associations differed significantly across pregnancy trimesters.

Table S6. Sensitivity analysis for associations between urinary haloacetic acid concentrations (tertiles or categories) and risk of small for gestational age, low birthweight, and preterm birth, using SG-corrected concentrations to correct for urine dilution.[a]							
Biomarkers	First trimester		Second trimester		Third trimester		Type 3 P-Value[b]
	RR (95% CI)	n/N	RR (95% CI)	n/N	RR (95% CI)	n/N	
Small for gestational age							
TCAA							0.78
T1(0.13-0.89 µg/L)	1.0	21/456	1.0	14/291	1.0	18/309	
T2(0.89-1.46 µg/L)	1.45 (0.80, 2.64)	24/358	0.89 (0.43, 1.83)	16/369	0.50 (0.23, 1.09)	10/332	
T3(>1.46 µg/L)	0.75 (0.37, 1.52)	13/379	1.06 (0.54, 2.08)	21/411	1.39 (0.72, 2.71)	19/245	
P-trend	0.52		0.83		0.37		
DCAA							0.76
T1(0.27-3.87 µg/L)	1.0	21/507	1.0	11/283	1.0	14/267	
T2(3.87-5.82 µg/L)	1.38 (0.74, 2.59)	20/353	1.52 (0.73, 3.17)	22/374	1.33 (0.68, 2.62)	22/330	
T3(>5.82 µg/L)	1.25 (0.65, 2.39)	17/333	1.10 (0.52, 2.34)	18/414	0.72 (0.33, 1.61)	11/289	
P-trend	0.48		0.94		0.44		
Low birthweight							
TCAA							0.36
T1(0.13-0.89 µg/L)	1.0	14/527	1.0	10/347	1.0	10/359	
T2(0.89-1.46 µg/L)	1.13(0.52, 2.44)	13/422	0.74(0.30, 1.82)	9/414	0.60 (0.22, 1.65)	6/374	
T3(>1.46 µg/L)	0.41 (0.15, 1.16)	5/449	0.77 (0.33, 1.83)	11/487	1.08 (0.42, 2.80)	8/289	
P-trend	0.12		0.58		0.95		
DCAA							0.52
T1(0.27-3.87 µg/L)	1.0	16/597	1.0	6/333	1.0	7/306	
T2(3.87-5.82 µg/L)	0.96(0.43, 2.15)	10/409	1.54 (0.58, 4.14)	12/426	1.04 (0.39, 2.83)	9/387	
T3(>5.82 µg/L)	0.63 (0.24, 1.63)	6/392	1.40 (0.52, 3.74)	12/489	1.16(0.41, 3.26)	8/329	
P-trend	0.37		0.56		0.78		
Preterm birth							

TCAA							0.45
T1(0.13-0.89 µg/L)	1.0	21/556	1.0	15/366	1.0	10/379	
T2(0.89-1.46 µg/L)	1.01 (0.53, 1.92)	17/453	0.97 (0.49, 1.92)	18/443	1.42 (0.64, 3.17)	15/406	
T3(>1.46 µg/L)	0.96 (0.50, 1.83)	17/481	0.70 (0.34, 1.43)	15/519	1.712 (0.75, 4.02)	13/304	
P-trend	0.90		0.31		0.19		
DCAA							0.67
T1(0.27-3.87 µg/L)	1.0	23/628	1.0	13/350	1.0	12/325	
T2(3.87-5.82 µg/L)	1.46 (0.81, 2.65)	22/441	1.13(0.56, 2.30)	19/449	1.01 (0.47, 2.14)	16/410	
T3(>5.82 µg/L)	0.67 (0.32, 2.65)	10/421	0.82 (0.39, 1.70)	16/529	0.73 (0.31, 1.72)	10/354	
P-trend	0.45		0.54		0.48		

Abbreviations: TCM, chloroform; BDCM, bromodichloromethane; DBCM, dibromochloromethane; TBM, bromoform; DCAA, dichloroacetic acid; TCAA, trichloroacetic acid; Br-THM, brominated trihalomethanes; TTHMs, total trihalomethanes; THMs, trihalomethanes; HAAs, haloacetic acids; n, numerator for cases of study outcome; N, total number of participants per subgroup. First trimester: gestational age <14 weeks; mean, 9.2±2.3 weeks. Second trimester: gestational age 14-27 weeks; mean, 17.1±2.0 weeks. Third trimester: gestational age >27 weeks; mean 31.8±2.3 weeks). [a]Adjusted for maternal age, body mass index at recruitment, household income, active/passive smoking status, gestational age at sampling, the time of day of sample collection, infant sex, and delivery model. [b]Type 3 tests were conducted based on multiple informant models by fitting generalized estimating equations with a log link function and Poisson distribution; a Type 3 p-value of <0.10 indicated that the associations differed significantly across pregnancy trimesters.

Table S7. Proportion of adverse birth outcomes of included versus excluded women due to missing measurements of blood THMs during the third trimester.		
Outcomes	Measured (n=1113)	Missing (n=547)
Small for gestational age		
Yes	46	17
No	1067	530
Prevalence	4.1%	3.1%
Low birth weight		
Yes	26	8
No	1087	539
Prevalence	2.3%	1.5%
Preterm birth		
Yes	39	20
No	1074	527
Prevalence	3.5%	3.7%