## **Online Data Supplement**

Association of blood trihalomethane concentrations with asthma in U.S.

adolescents: nationally representative cross-sectional study

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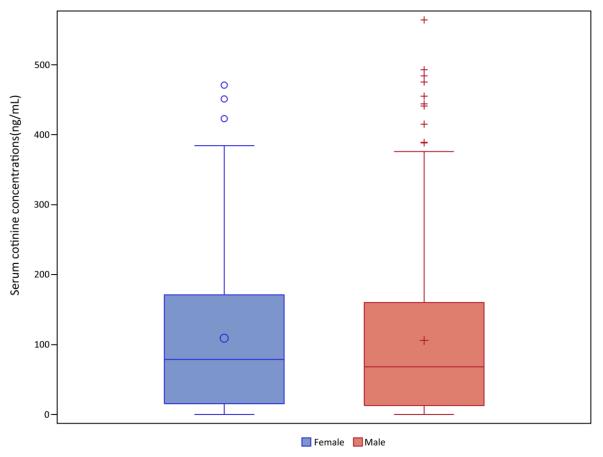


Figure S1. Distribution of serum cotinine concentrations (ng/mL) according to sex among participants with tobacco smoke exposure (NHANES, 2005-2012). The displayed values are the 10th (bottom whisker), 25th percentile (bottom of the box), median (line in box), 75th percentile (top of the box), and 90th (top whisker) of the concentrations. P for the Wilcoxon Rank-Sum Test > 0.05.

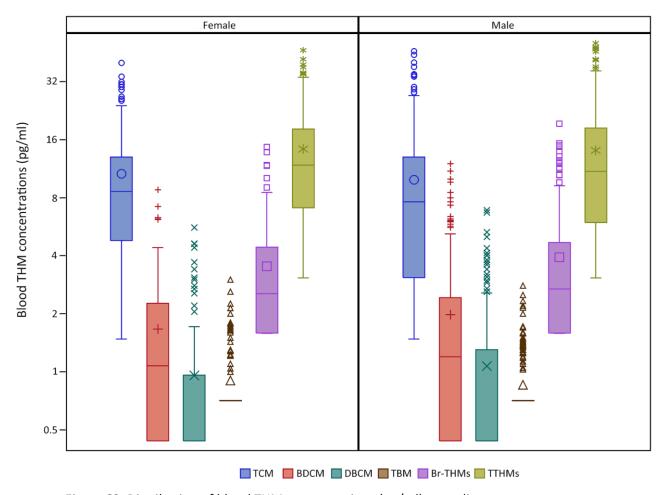


Figure S2. Distribution of blood THM concentrations (pg/ml) according to sex among participants with tobacco smoke exposure (NHANES, 2005-2012). The displayed values are the 10th (bottom whisker), 25th percentile (bottom of the box), median (line in box), 75th percentile (top of the box), and 90th (top whisker) of the concentrations. *P* for the Wilcoxon Rank-Sum Test all > 0.05. Abbreviations: THM, trihalomethane; TCM, chloroform; BDCM, bromodichloromethane; DBCM, dibromochloromethane; TBM, bromoform; Br-THMs, the sum of BDCM, DBCM, and TBM; TTHMs, the sum of TCM and Br-THMs.

Table S1. Characteristics of included adolescents and those excluded for study participants in NHANES

2005-2012 [mean (95% CI) or N (%)].<sup>a</sup>

| 2005-2012 [mean (95% CI) or N  | Included participants | Excluded participants | P-value <sup>b</sup> |
|--------------------------------|-----------------------|-----------------------|----------------------|
| Characteristic                 | (n=2,359)             | (n=3,779)             | P-value              |
| Survey cycle                   |                       |                       |                      |
| 2005-2006                      | 882 (24.7)            | 1,406 (25.1)          |                      |
| 2007-2008                      | 457 (24.3)            | 781 (25.5)            | 0.89                 |
| 2009-2010                      | 526 (25.2)            | 813 (24.4)            |                      |
| 2011-2012                      | 494 (25.7)            | 779 (25.0)            |                      |
| Age, years                     | 15.5 (15.4, 15.6)     | 15.4 (15.3, 15.5)     | 0.21                 |
| BMI Z - score                  | 0.62 (0.57, 0.67)     | 0.51 (0.44, 0.57)     | 0.002                |
| Sex                            |                       |                       |                      |
| Male                           | 1,202 (49.9)          | 1,940 (51.6)          | 0.29                 |
| Female                         | 1,157 (50.1)          | 1,839 (48.4)          |                      |
| Race/ethnicity                 | , , ,                 | , , ,                 |                      |
| Non-Hispanic White             | 641 (58.6)            | 1,053 (59.5)          |                      |
| Non-Hispanic Black             | 684 (14.9)            | 1,107 (15.0)          | 0.44                 |
| Mexican American               | 646 (13.5)            | 969 (12.1)            |                      |
| Other                          | 388 (13.0)            | 650 (13.4)            |                      |
| Family income-poverty ratio    | (,                    | ,                     |                      |
| 0-1.0                          | 734 (23.4)            | 1,051 (21.6)          |                      |
| 1.1-3.0                        | 859 (35.6)            | 1,461 (39.3)          | 0.13                 |
| >3.0                           | 612 (41.0)            | 930 (39.1)            |                      |
| Leisure-time physical activity | 012 (11.0)            | 330 (33.1)            |                      |
| (hours per week)               |                       |                       |                      |
| < 3                            | 1,032 (39.6)          | 1,477 (39.8)          | 0.80                 |
| 3-7                            | 539 (25.3)            | 817 (24.2)            |                      |
| >7                             | 778 (35.0)            | 1,185 (36.0)          |                      |
| Current allergic conditions    | - (,                  | , ( ,                 |                      |
| Yes                            | 630 (27.0)            | 952 (25.0)            | 0.31                 |
| No                             | 1,729 (73.0)          | 2,827 (75.0)          |                      |
| Examination session            | 1,723 (73.0)          | 2,027 (73.0)          |                      |
| Morning                        | 1,174 (50.4)          | 1,695 (47.6)          |                      |
| Afternoon                      | 777 (31.7)            | 1,203 (32.2)          | 0.71                 |
| Evening                        | 408 (17.9)            | 700 (20.2)            |                      |
| Sampling season                | 400 (17.5)            | 700 (20.2)            |                      |
| November through April         | 1,222 (42.9)          | 1,819 (44.2)          | 0.50                 |
| May through October            | 1,137 (50.1)          | 1,779 (55.8)          | 0.50                 |
| Family history of asthma       | 1,13, (30.1)          | 1, (55.0)             |                      |
| Yes                            | 455 (21.9)            | 710 (22.1)            | 0.89                 |
| No                             | 1,904 (78.1)          | 3,069 (77.9)          | 0.03                 |
| Ever (lifetime) asthma         | _,55 . (, 5.12)       | 2,222 ( )             |                      |
| Yes                            | 441 (20.3)            | 722 (19.6)            | 0.69                 |
| Never                          | 1,918 (79.7)          | 3,057 (80.4)          | 0.03                 |
| Current asthma                 | 1,515 (75.7)          | 3,037 (30.1)          |                      |
| Yes                            | 196 (9.1)             | 272 (7.7)             | 0.20                 |
| No                             | 2,163 (90.9)          | 3,507 (92.3)          | 5.20                 |

Mean (95% CI) and N (%) were accounted for complex, multistage sampling survey designs (e.g., sampling weights, stratification, and clusters) to ensure nationally representative estimation.

<sup>&</sup>lt;sup>a</sup> A total of 31, 491, and 310 participants had missing information on BMI Z - score, family income-poverty ratio, and levels of leisure-time physical activity, respectively; data on water-use activities was only collected among participants who were measured for blood volatile organic compounds.

<sup>b</sup> P-value was calculated by Rao-Scott chi-square test and t-test for categorical and continuous variables.

Table S2. Characteristics of study participants in NHANES 2005-2012 according to quartiles of blood TTHM concentrations [mean (95% CI) or N (%)].

|   |                   |                   | Blood TTHM        |                   |                |
|---|-------------------|-------------------|-------------------|-------------------|----------------|
| <b>Characteristic</b> <sup>a</sup>          | Quartile 1        | Quartile 2        | Quartile 3        | Quartile4         | P <sup>b</sup> |
|   | (n=540)           | (n=540)           | (n=541)           | (n=540)           | P              |
| Survey cycle                                |                   |                   |                   |                   |                |
| 2005-2006                                   | 138 (17.4)        | 202 (23.3)        | 234 (31.3)        | 219 (27.7)        |                |
| 2007-2008                                   | 133 (28.0)        | 99 (21.1)         | 91 (22.7)         | 90 (23.5)         | < 0.001        |
| 2009-2010                                   | 117 (17.5)        | 123 (23.9)        | 121 (25.9)        | 147 (32.1)        |                |
| 2011-2012                                   | 152 (37.1)        | 116 (31.7)        | 95 (20.1)         | 84 (16.7)         |                |
| Age, years                                  | 15.5 (15.3, 15.8) | 15.4 (15.2, 15.7) | 15.5 (15.2, 15.8) | 15.4 (15.2, 15.7) | 0.94           |
| BMI Z - score                               | 0.55 (0.44, 0.67) | 0.66 (0.51, 0.81) | 0.64 (0.52, 0.77) | 0.62 (0.50, 0.75) | 0.61           |
| Sex   |                   |                   |                   |                   |                |
| Male  | 290 (50.5)        | 262 (49.2)        | 264 (48.7)        | 273 (55.4)        | 0.42           |
| Female                                      | 250 (49.5)        | 278 (50.8)        | 277 (51.3)        | 267 (44.6)        |                |
| Race/ethnicity                              |                   |                   |                   |                   |                |
| Non-Hispanic White                          | 205 (68.3)        | 138 (57.6)        | 126 (52.0)        | 123 (50.5)        |                |
| Non-Hispanic Black                          | 112 (9.5)         | 171 (16.3)        | 177 (18.8)        | 186 (20.2)        | < 0.001        |
| Mexican American                            | 138 (11.8)        | 136 (12.6)        | 151 (14.7)        | 143 (14.2)        |                |
| Other                                       | 85 (10.4)         | 95 (13.5)         | 87 (14.5)         | 88 (15.1)         |                |
| Family income-poverty ratio                 |                   |                   |                   |                   |                |
| 0-1.0                                       | 146 (19.5)        | 177 (25.2)        | 173 (24.8)        | 187 (27.8)        | 0.45           |
| 1.1-3.0                                     | 199 (34.5)        | 198 (36.0)        | 191 (33.2)        | 187 (37.0)        | 0.15           |
| >3.0  | 163 (46.0)        | 132 (38.8)        | 138 (42.0)        | 125 (35.2)        |                |
| Leisure-time physical activity level (hours | , ,               | ,                 | ,                 | , ,               |                |
| per week)                                   |                   |                   |                   |                   |                |
| < 3   | 242 (40.9)        | 241 (38.7)        | 230 (36.0)        | 254 (43.4)        | 0.79           |
| 3-7   | 132 (24.6)        | 115 (24.7)        | 126 (27.6)        | 121 (23.9)        |                |
| >7  | 164 (34.4)        | 182 (36.6)        | 183 (36.3)        | 172 (32.7)        |                |
| Current allergic conditions                 | . ,               |                   |                   |                   |                |
| Yes   | 140 (29.3)        | 141 (23.3)        | 156 (27.6)        | 137 (27.4)        | 0.46           |
| No  | 400 (70.7)        | 399 (76.7)        | 385 (72.4)        | 403 (72.6)        |                |
| Examination session                         |                   |                   |                   |                   | 0.33           |

| Morning                                 | 256 (50.1) | 248 (47.4) | 258 (49.7) | 319 (58.2) |         |
|---|------------|------------|------------|------------|---------|
| Afternoon                               | 181 (31.8) | 185 (34.1) | 187 (32.8) | 155 (28.7) |         |
| Evening                                 | 103 (18.1) | 107 (18.5) | 96 (17.5)  | 66 (13.1)  |         |
| Time interval since last shower or bath |            |            |            |            |         |
| (hour)                                  |            |            |            |            |         |
| ≤ 2                                     | 51 (11.7)  | 45 (12.2)  | 89 (17.7)  | 111 (20.0) | < 0.001 |
| 3-6                                     | 90 (17.0)  | 128 (22.5) | 127 (23.0) | 189 (36.1) | < 0.001 |
| 7-14                                    | 153 (30.6) | 144 (24.7) | 137 (23.6) | 102 (17.5) |         |
| > 14                                    | 246 (40.7) | 223 (40.6) | 188 (35.7) | 138 (26.4) |         |
| Sampling season                         |            |            |            |            |         |
| November 1 through April 30             | 251 (36.1) | 245 (55.7) | 267 (40.4) | 291 (47.1) | 0.15    |
| May 1 through October 31                | 289 (63.9) | 295 (44.3) | 274 (59.6) | 249 (52.9) |         |
| Swimming pool/hot tub/ steam room use   |            |            |            |            |         |
| within 72h                              |            |            |            |            | 0.04    |
| Yes                                     | 18 (5.6)   | 32 (10.7)  | 25 (8.7)   | 43 (12.8)  | 0.04    |
| No                                      | 522 (94.4) | 508 (89.3) | 516 (91.3) | 497 (87.2) |         |

Abbreviations: TCM, chloroform; BDCM, bromodichloromethane; DBCM, dibromochloromethane; TBM, bromoform; Br-THMs, the sum of BDCM, DBCM, and TBM; TTHMs, the sum of TCM and Br-THMs.

All estimates were accounted for complex survey designs.

<sup>&</sup>lt;sup>a</sup> A total of 30, 150, and 9 participants had missing information on BMI Z - score, family income-poverty ratio, and Leisure-time physical activity level, respectively.

b P-value was calculated by Rao-Scott chi-square test and t-test for categorical and continuous variables, respectively.

Table S3. Adjusted ORs (95% CIs) of ever asthma and current asthma in relation to blood THM concentrations among U.S.

adolescents with tobacco smoke exposure (n = 378), stratified by sex (NHANES, 2005-2012).<sup>a</sup>

| Blood THMs                                 |   | Ever asthma               |             | С                           | urrent asthma <sup>c</sup> |             |
|--|---|---------------------------|-------------|-----------------------------|----------------------------|-------------|
| (pg/ml)                                    | Male                                    | Female                    | P for       | Male                        | Female                     | P for       |
|  | (n = 240)                               | (n = 138)                 | interaction | (n = 212)                   | (n = 118)                  | interaction |
| TCM  | D - C                                   | D - (                     |             | D - (                       | D - C                      |             |
| Q1 (1.48-4.11)                             | Ref.                                    | Ref.                      |             | Ref.                        | Ref.                       |             |
| Q2 (4.12-8.34)                             | 0.73 (0.27, 1.93)                       | 0.43 (0.11, 1.78)         | 0.11        | 1.90 (0.20, 18.07)          | 0.47 (0.04, 6.12)          | 0.01        |
| Q3 (8.35-16.90)                            | 0.62 (0.20, 1.93)                       | 0.12 (0.02, 0.80)         |             | 3.52 (0.43, 28.65)          | 0.05 (0.001, 1.93)         |             |
| Q4 (> 16.90)                               | 1.89 (0.74, 4.84)                       | 0.37 (0.11, 1.32)         |             | 6.23 (1.25, 31.09)          | 0.13 (0.006, 2.66)         |             |
| P for trend <sup>b</sup>                   | 0.15                                    | 0.27                      |             | 0.002                       | 0.19                       |             |
| BDCM                                       | Def                                     | Def                       |             | Def                         | Det                        |             |
| T1 (0.44-0.75)                             | Ref.                                    | Ref.                      | 0.55        | Ref.                        | Ref.                       | 0.00        |
| T2 (0.76-2.50)                             | 0.83 (0.23, 3.02)                       | 1.04 (0.47, 2.32)         | 0.55        | 1.18 (0.19, 7.49)           | 4.12 (1.46, 11.65)         | 0.08        |
| T3 (> 2.50)                                | 1.82 (0.75, 4.47)                       | 0.86 (0.25, 2.98)         |             | 4.75 (1.29, 17.49)          | 1.52 (0.18, 12.88)         |             |
| P for trend <sup>b</sup>                   | 0.10                                    | 0.80                      |             | 0.008                       | 0.98                       |             |
| <b>DBCM</b> < 50 <sup>th</sup> (0.44-0.65) | Ref.                                    | Ref.                      |             | Ref.                        | Ref.                       |             |
| 50-75 <sup>th</sup> (0.66-1.87)            |   |                           | 0.10        |                             |                            | 0.11        |
| > 75 <sup>th</sup> (>1.87)                 | 1.34 (0.52, 3.45)<br>5.96 (2.79, 12.73) | 1.62 (0.54, 4.85)         | 0.10        | 1.93 (0.59, 6.28)           | 5.93 (1.61, 21.85)         | 0.11        |
| P for trend <sup>b</sup>                   | < 0.001                                 | 1.90 (0.53, 6.81)<br>0.39 |             | 7.57 (2.21, 25.89)<br>0.001 | 2.11 (0.22, 20.19)<br>0.74 |             |
| TBM  | < 0.001                                 | 0.59                      |             | 0.001                       | 0.74                       |             |
| < 75 <sup>th</sup> (0.71-1.13)             | Ref.                                    | Ref.                      |             | Ref.                        | Ref.                       |             |
| 75-87.5 <sup>th</sup>                      | ivei.                                   | ivei.                     |             | ivei.                       | ivei.                      |             |
| (1.14-2.10)                                | 2.65 (1.05, 6.68)                       | 1.06 (0.20, 5.66)         | 0.87        | 0.60 (0.15, 2.46)           | 1.25 (0.12, 12.67)         | 0.83        |
| > 87.5 <sup>th</sup> (> 2.10)              | 1.12 (0.23, 5.55)                       | 2.28 (0.53, 9.79)         |             | 1.29 (0.28, 5.93)           | 1.36 (0.12, 15.43)         |             |
| P for trend <sup>b</sup>                   | 0.82                                    | 0.29                      |             | 0.76                        | 0.78                       |             |
| Br-THMs                                    | 0.02                                    | 0.23                      |             | 0.70                        | 0.70                       |             |
| Q1 (1.58-1.78)                             | Ref.                                    | Ref.                      |             | Ref.                        | Ref.                       |             |
| Q2 (1.79-3.15)                             | 1.22 (0.39, 3.79)                       | 1.15 (0.30, 4.37)         |             | 2.42 (0.55, 10.92)          | 0.96 (0.27, 3.48)          |             |
| Q3 (3.16-6.69)                             | 0.84 (0.21, 3.30)                       | 0.91 (0.21, 3.60)         | 0.22        | 1.33 (0.54, 3.28)           | 1.75 (0.39, 7.74)          | 0.11        |
| Q4 (> 6.69)                                | 4.25 (1.69, 10.72)                      | 1.72 (0.39, 7.56)         |             | 9.63 (4.00, 23.23)          | 2.16 (0.28, 16.88)         |             |
| P for trend <sup>b</sup>                   | < 0.001                                 | 0.43                      |             | 0.002                       | 0.48                       |             |
| TTHMs                                      | 10.002                                  | 0.13                      |             | 0.002                       | 0.10                       |             |
| Q1 (3.07-6.99)                             | Ref.                                    | Ref.                      |             | Ref.                        | Ref.                       |             |
| Q2 (7.00-12.97)                            | 0.46 (0.17, 1.23)                       | 0.40 (0.16, 1.00)         |             | 0.86 (0.15, 4.85)           | 0.55 (0.11, 2.75)          |             |
| Q3 (12.98-25.63)                           | 0.45 (0.16, 1.27)                       | 0.21 (0.03, 1.32)         | 0.10        | 3.31 (1.23, 8.92)           | 0.36 (0.03, 5.09)          | 0.02        |
| Q4 (> 25.63)                               | 2.53 (1.20, 5.34)                       | 0.45 (0.12, 1.66)         |             | 6.72 (3.52, 12.80)          | 0.27 (0.04, 2.10)          |             |
| P for trend <sup>b</sup>                   | 0.005                                   | 0.38                      |             | <0.001                      | 0.27                       |             |

<sup>&</sup>lt;sup>a</sup> All models adjusted for age, race/ethnicity, BMI Z-score, family income-poverty ratio, family history of asthma, swimming

pool/hot tub/ steam room use within 72h, and survey cycle.

b Tests for linear trend were conducted by modeling categories of THM concentrations as ordinal variables using the median values within each category.

<sup>&</sup>lt;sup>c</sup> Participants who ever received a diagnosis of asthma but no wheezing or whistling in the past year were excluded in the model for current asthma (n = 48).

Table S4. Sensitivity analyses of the associations between **ever** asthma and blood THM concentrations among U.S. adolescents according to tobacco smoke exposure, excluding participants with missing data on BMI z-scores or family income-poverty ratio (NHANES, 2005-2012).<sup>a,b</sup>

| Blood THMs (pg/ml)                | All <sup>d</sup><br>(N=2,176) | Tobacco smoke<br>exposure<br>(n = 351) | No tobacco smoke<br>exposure<br>(n = 1,825) | P for interaction |
|-----------------------------------|-------------------------------|--|---|-------------------|
| TCM                               |                               |  |   |                   |
| Q1 (1.48-4.11)                    | Ref.                          | Ref.                                   | Ref.  |                   |
| Q2 (4.12-8.34)                    | 0.76 (0.55, 1.03)             | 0.90 (0.41, 1.98)                      | 0.71 (0.50, 1.02)                           | 0.32              |
| Q3 (8.35-16.90)                   | 0.77 (0.50, 1.20)             | 0.59 (0.23, 1.49)                      | 0.82 (0.49, 1.36)                           | 0.32              |
| Q4 (> 16.90)                      | 0.80 (0.53, 1.19)             | 1.36 (0.51, 3.63)                      | 0.71 (0.47, 1.07)                           |                   |
| P for trend <sup>c</sup>          | 0.47                          | 0.43                                   | 0.25  |                   |
| BDCM                              |                               |  |   |                   |
| T1 (0.44-0.75)                    | Ref.                          | Ref.                                   | Ref.  |                   |
| T2 (0.76-2.50)                    | 0.79 (0.54, 1.17)             | 1.13 (0.47, 2.71)                      | 0.72 (0.46, 1.12)                           | 0.03              |
| T3 (> 2.50)                       | 0.93 (0.67, 1.27)             | 1.89 (0.85, 4.19)                      | 0.79 (0.57, 1.09)                           |                   |
| P for trend <sup>c</sup>          | 0.90                          | 0.10                                   | 0.27  |                   |
| DBCM                              |                               |  |   |                   |
| < 50 <sup>th</sup> (0.44-0.65)    | Ref.                          | Ref.                                   | Ref.  |                   |
| 50-75 <sup>th</sup> (0.66-1.87)   | 1.03 (0.67, 1.57)             | 1.67 (0.76, 3.66)                      | 0.93 (0.56, 1.56)                           | 0.03              |
| > 75 <sup>th</sup> ( > 1.87)      | 1.54 (1.08, 2.18)             | 4.31 (2.00, 9.29)                      | 1.27 (0.85, 1.90)                           |                   |
| P for trend <sup>c</sup>          | 0.01                          | < 0.001                                | 0.18  |                   |
| TBM                               |                               |  | _ ^   |                   |
| < 75 <sup>th</sup> (0.71-1.13)    | Ref.                          | Ref.                                   | Ref.  |                   |
| 75-87.5 <sup>th</sup> (1.14-2.10) | 1.45 (0.93, 2.26)             | 1.58 (0.64, 3.90)                      | 1.49 (0.88, 2.52)                           | 0.98              |
| > 87.5 <sup>th</sup> (> 2.10)     | 1.12 (0.61, 2.03)             | 1.38 (0.46, 4.11)                      | 1.13 (0.63, 2.04)                           |                   |
| P for trend <sup>c</sup>          | 0.59                          | 0.40                                   | 0.59  |                   |
| Br-THMs                           | 5.6                           | 5 (                                    | 5. (  |                   |
| Q1 (1.58-1.78)                    | Ref.                          | Ref.                                   | Ref.  |                   |
| Q2 (1.79-3.15)                    | 1.01 (0.65, 1.54)             | 1.44 (0.57, 3.65)                      | 0.87 (0.51, 1.49)                           | 0.02              |
| Q3 (3.16-6.69)                    | 0.86 (0.58, 1.28)             | 1.27 (0.40, 3.99)                      | 0.80 (0.51, 1.27)                           |                   |
| Q4 (> 6.69)                       | 1.39 (0.94, 2.07)             | 3.57 (1.52, 8.41)                      | 1.10 (0.71, 1.70)                           |                   |
| P for trend <sup>c</sup>          | 0.07                          | 0.003                                  | 0.41  |                   |
| TTHMs                             | Def                           | Det                                    | Det   |                   |
| Q1 (3.07-6.99)                    | Ref.                          | Ref.                                   | Ref.  |                   |
| Q2 (7.00-12.97)                   | 0.56 (0.37, 0.85)             | 0.58 (0.27, 2.52)                      | 0.54 (0.34, 0.86)                           | 0.14              |
| Q3 (12.98-25.63)                  | 0.72 (0.46, 1.13)             | 0.56 (0.22, 1.38)                      | 0.80 (0.49, 1.31)                           |                   |
| Q4 (> 25.63)                      | 0.89 (0.57, 1.39)             | 1.58 (0.72, 3.48)                      | 0.79 (0.50, 1.23)                           |                   |
| P for trend <sup>c</sup>          | 0.89                          | 0.09                                   | 0.70  |                   |

<sup>&</sup>lt;sup>a</sup> All models adjusted for age, sex, race/ethnicity, BMI *Z*-score, family income-poverty ratio, family history of asthma, swimming pool/hot tub/ steam room use within 72h, and survey cycle.

<sup>&</sup>lt;sup>b</sup> Participants with missing data on BMI z-scores or family income-poverty ratio (n =185) were excluded.

<sup>&</sup>lt;sup>c</sup> Tests for linear trend were conducted by modeling categories of THM concentrations as ordinal variables using the median values within each category.

<sup>&</sup>lt;sup>d</sup> Models were additionally adjusted for tobacco smoke exposure.

Table S5. Sensitivity analyses of the associations between **ever** asthma and blood THM concentrations among U.S. adolescents according to tobacco smoke exposure with additional adjustment for specific covariates related to THM exposures (NHANES, 2005-2012).<sup>a</sup>

| Blood THMs (pg/ml)                | All <sup>c</sup><br>(N=2,359) | Tobacco smoke<br>exposure<br>(n = 378) | No tobacco smoke<br>exposure<br>(n = 1,981) | P for interaction |
|-----------------------------------|-------------------------------|--|---|-------------------|
| TCM                               |                               |  |   |                   |
| Q1 (1.48-4.11)                    | Ref.                          | Ref.                                   | Ref.  |                   |
| Q2 (4.12-8.34)                    | 0.74 (0.55, 1.01)             | 0.80 (0.37, 1.70)                      | 0.71 (0.49, 1.02)                           | 0.29              |
| Q3 (8.35-16.90)                   | 0.79 (0.51, 1.22)             | 0.52 (0.22, 1.25)                      | 0.86 (0.53, 1.41)                           | 0.29              |
| Q4 (> 16.90)                      | 0.77 (0.51, 1.22)             | 1.16 (0.48, 2.81)                      | 0.70 (0.46, 1.07)                           |                   |
| P for trend <sup>b</sup>          | 0.40                          | 0.58                                   | 0.24  |                   |
| BDCM                              |                               |  |   |                   |
| T1 (0.44-0.75)                    | Ref.                          | Ref.                                   | Ref.  |                   |
| T2 (0.76-2.50)                    | 0.80 (0.56, 1.16)             | 0.84 (0.38, 1.89)                      | 0.74 (0.49, 1.13)                           | 0.05              |
| T3 (> 2.50)                       | 0.89 (0.64, 1.23)             | 1.54 (0.68, 3.49)                      | 0.77 (0.54, 1.09)                           |                   |
| P for trend <sup>b</sup>          | 0.65                          | 0.23                                   | 0.23  |                   |
| DBCM                              |                               |  |   |                   |
| < 50 <sup>th</sup> (0.44-0.65)    | Ref.                          | Ref.                                   | Ref.  |                   |
| 50-75 <sup>th</sup> (0.66-1.87)   | 0.96 (0.61, 1.51)             | 1.61 (0.73, 3.56)                      | 0.85 (0.51, 1.42)                           | 0.03              |
| > 75 <sup>th</sup> ( > 1.87)      | 1.47 (1.02, 2.12)             | 3.86 (1.75, 8.49)                      | 1.20 (0.78, 1.84)                           |                   |
| P for trend <sup>b</sup>          | 0.02                          | 0.001                                  | 0.29  |                   |
| TBM                               |                               |  |   |                   |
| < 75 <sup>th</sup> (0.71-1.13)    | Ref.                          | Ref.                                   | Ref.  |                   |
| 75-87.5 <sup>th</sup> (1.14-2.10) | 1.38 (0.87, 2.19)             | 1.49 (0.63, 3.53)                      | 1.37 (0.79, 2.37)                           | 0.99              |
| > 87.5 <sup>th</sup> (> 2.10)     | 1.16 (0.66, 2.04)             | 1.26 (0.43, 3.69)                      | 1.18 (0.68, 2.05)                           |                   |
| P for trend <sup>b</sup>          | 0.53                          | 0.51                                   | 0.51  |                   |
| Br-THMs                           | _                             | _                                      |   |                   |
| Q1 (1.58-1.78)                    | Ref.                          | Ref.                                   | Ref.  |                   |
| Q2 (1.79-3.15)                    | 1.02 (0.67, 1.56)             | 1.19 (0.48, 2.96)                      | 0.90 (0.54, 1.50)                           | 0.02              |
| Q3 (3.16-6.69)                    | 0.87 (0.58, 1.31)             | 0.98 (0.36, 2.65)                      | 0.81 (0.51, 1.29)                           | 0.02              |
| Q4 (> 6.69)                       | 1.37 (0.91, 2.08)             | 3.10 (1.30, 2.65)                      | 1.10 (0.69, 1.75)                           |                   |
| P for trend <sup>b</sup>          | 0.08                          | 0.008                                  | 0.24  |                   |
| TTHMs                             |                               | _ •                                    |   |                   |
| Q1 (3.07-6.99)                    | Ref.                          | Ref.                                   | Ref.  |                   |
| Q2 (7.00-12.97)                   | 0.57 (0.38, 0.86)             | 0.46 (0.21, 1.03)                      | 0.56 (0.36, 0.87)                           | 0.19              |
| Q3 (12.98-25.63)                  | 0.74 (0.48, 1.15)             | 0.46 (0.19, 1.13)                      | 0.85 (0.53, 1.36)                           | 5.25              |
| Q4 (> 25.63)                      | 0.85 (0.54, 1.35)             | 1.13 (0.51, 2.50)                      | 0.78 (0.49, 1.23)                           |                   |
| P for trend <sup>b</sup>          | 0.97                          | 0.32                                   | 0.68  |                   |

<sup>&</sup>lt;sup>a</sup> All models adjusted for age, sex, race/ethnicity, BMI *Z*-score, family income-poverty ratio, family history of asthma, examination session, sampling season, and the time interval since last shower or bath, swimming pool/hot tub/ steam room use within 72h, and survey cycle.
<sup>b</sup> Tests for linear trend were conducted by modeling categories of THM concentrations as ordinal variables using

<sup>&</sup>lt;sup>b</sup> Tests for linear trend were conducted by modeling categories of THM concentrations as ordinal variables using the median values within each category.

<sup>&</sup>lt;sup>c</sup> Models were additionally adjusted for tobacco smoke exposure.

Table S6. Sensitivity analyses of the associations between **ever** asthma and blood THM concentrations among U.S. adolescents according to tobacco smoke exposure with additional adjustment for levels of leisure-time physical activity and allergic symptoms (NHANES, 2005-2012).<sup>a</sup>

| Blood THMs (pg/ml)                | All <sup>c</sup><br>(N=2,359) | Tobacco smoke exposure | No tobacco smoke exposure | P for interaction |
|-----------------------------------|-------------------------------|------------------------|---------------------------|-------------------|
| TCM                               |                               | (n = 378)              | (n = 1,981)               |                   |
| Q1 (1.48-4.11)                    | Ref.                          | Ref.                   | Ref.                      |                   |
| Q2 (4.12-8.34)                    | 0.84 (0.62, 1.13)             | 0.95 (0.44, 2.06)      | 0.78 (0.55, 1.12)         |                   |
| Q3 (8.35-16.90)                   | 0.80 (0.49, 1.30)             | 0.54 (0.23, 1.25)      | 0.86 (0.48, 1.53)         | 0.17              |
| Q4 (> 16.90)                      | 0.86 (0.57, 1.31)             | 1.48 (0.63, 3.49)      | 0.75 (0.48, 1.17)         |                   |
| P for trend <sup>b</sup>          | 0.63                          | 0.30                   | 0.34                      |                   |
| BDCM                              | 0.03                          | 0.50                   | 0.5 1                     |                   |
| T1 (0.44-0.75)                    | Ref.                          | Ref.                   | Ref.                      |                   |
| T2 (0.76-2.50)                    | 0.93 (0.62, 1.38)             | 1.05 (0.41, 2.70)      | 0.87 (0.56, 1.37)         | 0.06              |
| T3 (> 2.50)                       | 1.03 (0.72, 1.47)             | 1.82 (0.77, 4.31)      | 0.89 (0.59, 1.33)         |                   |
| P for trend <sup>b</sup>          | 0.77                          | 0.12                   | 0.63                      |                   |
| DBCM                              |                               |                        |                           |                   |
| < 50 <sup>th</sup> (0.44-0.65)    | Ref.                          | Ref.                   | Ref.                      |                   |
| 50-75 <sup>th</sup> (0.66-1.87)   | 1.00 (0.65, 1.53)             | 1.57 (0.75, 3.31)      | 0.90 (0.55, 1.47)         | 0.04              |
| > 75 <sup>th</sup> ( > 1.87)      | 1.74 (1.18, 2.56)             | 4.92 (1.98, 12.17)     | 1.41 (0.90, 2.20)         |                   |
| P for trend <sup>b</sup>          | 0.004                         | 0.001                  | 0.09                      |                   |
| TBM                               |                               |                        |                           |                   |
| < 75 <sup>th</sup> (0.71-1.13)    | Ref.                          | Ref.                   | Ref.                      |                   |
| 75-87.5 <sup>th</sup> (1.14-2.10) | 1.50 (0.88, 2.55)             | 1.65 (0.68, 4.02)      | 1.49 (0.81, 2.72)         | 0.64              |
| > 87.5 <sup>th</sup> (> 2.10)     | 1.27 (0.76, 2.14)             | 1.61 (0.55, 4.75)      | 1.24 (0.74, 2.09)         |                   |
| P for trend <sup>b</sup>          | 0.27                          | 0.25                   | 0.35                      |                   |
| Br-THMs                           | 5.6                           | 5.6                    | 5.6                       |                   |
| Q1 (1.58-1.78)                    | Ref.                          | Ref.                   | Ref.                      |                   |
| Q2 (1.79-3.15)                    | 1.07 (0.67, 1.69)             | 1.43 (0.59, 3.46)      | 0.95 (0.54, 1.66)         | 0.03              |
| Q3 (3.16-6.69)                    | 1.01 (0.68, 1.49)             | 1.30 (0.40, 4.19)      | 0.93 (0.61, 1.43)         |                   |
| Q4 (> 6.69)                       | 1.57 (1.03, 2.38)             | 3.57 (1.37, 9.32)      | 1.24 (0.77, 1.99)         |                   |
| P for trend <sup>b</sup>          | 0.02                          | 0.006                  | 0.25                      |                   |
| <b>TTHMs</b><br>Q1 (3.07-6.99)    | Ref.                          | Ref.                   | Ref.                      |                   |
| Q2 (7.00-12.97)                   | 0.64 (0.43, 0.95)             | 0.62 (0.30, 1.27)      | 0.63 (0.42, 0.96)         |                   |
| Q3 (12.98-25.63)                  | 0.78 (0.48, 1.28)             | 0.49 (0.20, 1.20)      | 0.91 (0.52, 1.59)         | 0.12              |
| Q4 (> 25.63)                      | 0.76 (0.48, 1.28)             | 1.55 (0.67, 3.61)      | 0.83 (0.53, 1.30)         |                   |
| P for trend <sup>b</sup>          | 0.72                          | 0.14                   | 0.03 (0.33, 1.30)         |                   |

<sup>&</sup>lt;sup>a</sup> All models adjusted for age, sex, race/ethnicity, BMI *Z*-score, family income-poverty ratio, family history of asthma, levels of leisure-time physical activity, current allergic symptoms, and survey cycle.

<sup>&</sup>lt;sup>b</sup> Tests for linear trend were conducted by modeling categories of THM concentrations as ordinal variables using the median values within each category.

<sup>&</sup>lt;sup>c</sup> Models were additionally adjusted for tobacco smoke exposure.

Table S7. Sensitivity analyses of the associations between **ever** asthma and blood THM concentrations among U.S. adolescents according to tobacco smoke exposure, excluding participants who spent any time at a swimming pool, a hot tub, or a steam room in the past 72 hours (NHANES, 2005-2012).<sup>a</sup>

| Blood THMs (pg/ml)                      | All <sup>c</sup><br>(N=2,228) | Tobacco smoke<br>exposure<br>(n = 363) | No tobacco smoke<br>exposure<br>(n = 1,865) | P for interaction |
|---|-------------------------------|--|---|-------------------|
| TCM                                     |                               | (11 – 303)                             | (11 – 1,003)                                |                   |
| Q1 (1.48-4.11)                          | Ref.                          | Ref.                                   | Ref.  |                   |
| Q2 (4.12-8.34)                          | 0.80 (0.57, 1.12)             | 0.87 (0.42, 1.80)                      | 0.77 (0.51, 1.15)                           |                   |
| Q3 (8.35-16.90)                         | 0.81 (0.52, 1.26)             | 0.52 (0.21, 1.30)                      | 0.88 (0.53, 1.45)                           | 0.44              |
| Q4 (> 16.90)                            | 0.73 (0.48, 1.11)             | 1.16 (0.44, 3.11)                      | 0.66 (0.43, 1.02)                           |                   |
| P for trend <sup>b</sup>                | 0.22                          | 0.67                                   | 0.13  |                   |
| BDCM                                    |                               |  |   |                   |
| T1 (0.44-0.75)                          | Ref.                          | Ref.                                   | Ref.  |                   |
| T2 (0.76-2.50)                          | 0.87 (0.59, 1.30)             | 0.94 (0.42, 2.11)                      | 0.99 (0.61, 1.61)                           | 0.11              |
| T3 (> 2.50)                             | 0.92 (0.66, 1.28)             | 1.44 (0.65, 3.21)                      | 0.86 (0.57, 1.28)                           |                   |
| P for trend <sup>b</sup>                | 0.74                          | 0.30                                   | 0.33  |                   |
| DBCM                                    |                               |  |   |                   |
| < 50 <sup>th</sup> (0.44-0.65)          | Ref.                          | Ref.                                   | Ref.  |                   |
| 50-75 <sup>th</sup> (0.66-1.87)         | 1.02 (0.67, 1.55)             | 1.51 (0.72, 3.18)                      | 0.94 (0.57, 1.55)                           | 0.05              |
| > 75 <sup>th</sup> ( > 1.87)            | 1.51 (1.05, 2.18)             | 3.76 (1.76, 8.05)                      | 1.15 (0.76, 1.75)                           |                   |
| P for trend <sup>b</sup>                | 0.02                          | 0.002                                  | 0.17  |                   |
| TBM                                     |                               |  |   |                   |
| < 75 <sup>th</sup> (0.71-1.13)          | Ref.                          | Ref.                                   | Ref.  |                   |
| 75-87.5 <sup>th</sup> (1.14-2.10)       | 1.47 (0.93, 2.33)             | 1.74 (0.75, 4.05)                      | 1.11 (0.70, 1.75)                           | 0.50              |
| > 87.5 <sup>th</sup> (> 2.10)           | 1.35 (0.76, 2.40)             | 1.12 (0.31, 4.07)                      | 1.65 (0.97, 2.79)                           |                   |
| P for trend <sup>b</sup>                | 0.23                          | 0.60                                   | 0.15  |                   |
| Br-THMs                                 | 5 (                           | 5. (                                   | 5 (   |                   |
| Q1 (1.58-1.78)                          | Ref.                          | Ref.                                   | Ref.  |                   |
| Q2 (1.79-3.15)                          | 1.05 (0.70, 1.58)             | 1.47 (0.63, 3.43)                      | 0.93 (0.56, 1.53)                           | 0.14              |
| Q3 (3.16-6.69)                          | 0.93 (0.62, 1.37)             | 1.16 (0.42, 3.22)                      | 0.88 (0.55, 1.40)                           |                   |
| Q4 (> 6.69)<br>P for trend <sup>b</sup> | 1.39 (0.93, 2.09)             | 2.68 (1.12, 6.44)                      | 1.20 (0.78, 1.86)                           |                   |
| TTHMs                                   | 0.09                          | 0.03                                   | 0.25  |                   |
| Q1 (3.07-6.99)                          | Ref.                          | Ref.                                   | Ref.  |                   |
| Q2 (7.00-12.97)                         | 0.58 (0.38, 0.87)             | 0.53 (0.27, 1.07)                      | 0.58 (0.37, 0.90)                           |                   |
| Q3 (12.98-25.63)                        | 0.75 (0.48, 1.16)             | 0.47 (0.19, 1.19)                      | 0.87 (0.54, 1.38)                           | 0.55              |
| Q4 (> 25.63)                            | 0.80 (0.51, 1.26)             | 1.11 (0.45, 2.68)                      | 0.77 (0.49, 1.21)                           |                   |
| P for trend <sup>b</sup>                | 0.70                          | 0.53                                   | 0.58  |                   |

<sup>&</sup>lt;sup>a</sup> All models adjusted for age, sex, race/ethnicity, BMI *Z*-score, family income-poverty ratio, family history of asthma, and survey cycle.

<sup>&</sup>lt;sup>b</sup> Tests for linear trend were conducted by modeling categories of THM concentrations as ordinal variables using the median values within each category.

<sup>&</sup>lt;sup>c</sup> Models were additionally adjusted for tobacco smoke exposure.

Table S8. Water-use activities of study participants in NHANES 2005-2012 according to asthma history [N (%).

| Swimming pool/hot tub/<br>steam room use within 72h | Current asthma<br>(n = 196) | No asthma<br>(n=1,918) | P-value <sup>a</sup> |
|---|-----------------------------|------------------------|----------------------|
| Yes   | 10 (6.1)                    | 109 (9.4)              | 0.29                 |
| No  | 186 (93.9)                  | 1,809 (90.6)           | 0.29                 |

<sup>&</sup>lt;sup>a</sup> P-value was calculated by the Rao-Scott chi-square test.